

SCIENCE

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SHALL THEY SURVIVE?

By Dr. E. V. COWDRY

PROFESSOR OF ANATOMY, WASHINGTON UNIVERSITY MEDICAL SCHOOL; DIRECTOR OF RESEARCH, BARNARD FREE SKIN AND CANCER HOSPITAL, ST. LOUIS

ARE private colleges and universities in this country worth saving? If so, something effective must be done soon.

These institutions rely chiefly upon voluntary donations from private persons for their support. Some of these contributions, received in the early days, have been set aside as endowments from which they derive the interest. But what amounts to a social revolution has taken place since the depression, with its epidemic of bank failures and many other misfortunes. Income on investments has fallen so that institutions now receive only about half as much from their endowments, and a new spirit is abroad throughout the land of letting Uncle Sam provide for everything with tax money. The idea of volun-

tarily giving has become almost a thing of the past, except to the American Red Cross and War Chests.

Yet in the past these private educational institutions have made great contributions to the wealth of the nation in the training of leaders in business, in the professions and in science and letters. In addition, they have helped to keep education free from regimentation and governmental control. This freedom in higher education is a priceless national asset. We have seen the consequences of its absence in Europe in the rising tide of totalitarian philosophy and practice. We take pride, also, in our great American public-supported institutions, which at present operate likewise in an atmosphere of intellectual freedom. The continuance of their greatness

depends in no small measure upon their labor side by side with these private competitors, and healthy exchange of personnel and ideals between the two is for their common good.

Hence, it is clear that, in the interest of the public institutions and of the public generally, the private colleges and universities are worth saving. How imminent is their need for aid? How great is it? How can it be met? How can it be met without sacrifice of their freedom from governmental control?

The difficulty is that these great private educational institutions are highly individualistic and have never spoken with one voice on anything, the reason for which is not far to seek. It is because they differ so widely, like individuals, both in heredity and in environment. The great pioneers were firmly established chiefly in the Atlantic States by far-sighted, public-spirited citizens before tax-supported educational institutions took hold. These have much inherited wealth, and, backed by generation after generation of influential alumni, are complacent in their strength and unwilling to make common cause with their weaker and younger fellows. Size is, however, not a measure of excellence and survival may not depend entirely on performance.

Where little tax money goes to higher education the citizens, if they give any serious thought to the problem, will be more likely themselves to contribute freely. Concretely, the receipts by institutions of higher education per capita of total population from public sources (taxes) in Massachusetts in 1939-40 were less than in any other State of the Union, or only 64 cents. During the same year the private gifts per student enrolled in its colleges and universities amounted to \$47.72. The State of Connecticut was more generous on both counts, the receipts per capita from public funds were \$1.12, while private gifts of \$101.51 per student were considerably greater than in any other State.

In the West the reverse holds to the great disadvantage of private institutions. For example, in California, certainly not second to Massachusetts or Connecticut in the number of wealthy persons, the receipts per capita of total population from public sources were \$2.87, or more than four times that of Massachusetts and twice that of Connecticut, while the private gifts per student enrolled in this self-same year were only \$17.83, or about one third as much as in the Eastern States.

Thus, danger for private institutions lies in the fact that they must compete with publicly financed institutions in areas where the habit of private giving is lacking, as in California, and in numerous States in which but little private wealth is available. Some say: "Well, if they can't swim, let them sink," while

others are of the opinion that they should receive helping hand.

In 1941-42 the public institutions of higher education received for current "educational and general purposes" \$251,820,909 of government funds (federal, state and local); whereas, the private institutions received only \$18,885,751 in government support. Any day now legislation may be enacted increasing the federal contribution to several hundred million dollars. The only question considered seems to be: How can state and municipal universities and colleges receive these large sums without federal control of education? No anxiety is expressed as to what this would do to private universities and colleges. Yet for the public institutions alone to be aided would accelerate the decline of the private ones.

In 1931-32 public institutions served 41.8 per cent of the nation's students. Since then the number has steadily increased to 53.3 per cent. in 1939-40, the latest period for which figures are available. This shift of students from the private to the public institutions is likely to increase.

Marked inequality is evident in dependence on students' fees. The public institutions were able to operate in 1941-42 by deriving only 16.6 per cent of their budgets from payments by students; whereas, private institutions were compelled to collect 49.6 per cent. from this source.

The higher fees charged students by the private institutions are unavoidable, though they have more permanent endowment than the public ones. In 1940 a year in which only 1,440 institutions reported on endowment to the U. S. Office of Education, private educational institutions had \$1,482,234,105 of endowment, as compared with \$204,048,662 for public institutions. But the interest from this endowment has steadily decreased from 5 per cent. or better, to about 3 per cent., and because of business uncertainty and high taxes, financial aid given voluntarily is shrinking. This decrease in interest from endowments hits the private institutions harder than it does the public ones, because they are more largely dependent on it.

There is another factor which bears down more heavily on the private institutions than on public ones. During the depression sizeable government grants were made to the latter for new buildings and equipment, but not to the former. Consequently, the private institutions must compete under the double handicap of less income and inferior physical plants.

In order to justify the higher fees from students the private institutions must somehow give more to them than the public institutions do. This means that they must offer teaching of higher quality. The impulse to survive is a great incentive to improvement.

Gallant efforts are being made, and these institutions are bearing their share in the war effort.

The main problem centers in the teaching staff. Let us consider the condition of teaching employment in general, irrespective of whether it is in private or public institutions, before discussing the special handicaps existing in the former. Testimony was given last year by Dr. Robert P. Ludlum, representing the American Association of University Professors, at hearings before a subcommittee of the Committee on Education and Labor of the U. S. Senate. This testimony related to the staffs of both public and private institutions and brought out the fact, well known to the sufferers and quickly forgotten by the public, that the salary increases enjoyed by some have been small and quite insufficient to compensate for the great increase in the cost of living, while others are still laboring under the handicap of salary cuts made during the depression. But the names of the institutions still operating in whole or in part at the depression salary level were gracefully omitted.

No consideration of the general problem of salary is complete without emphasis on employability. In academic circles most individuals past forty years of age continue with their work, but increases in salary come to them slowly or not at all. They may have reached the peak; but "peak" is not the word, for it signifies something high. The point is that they are usually not in demand by other institutions, because the policy is widespread to seek out young and promising candidates for important posts. Consequently, those who are past forty carry on, but salary increases are not necessary to retain their services. It is doubtful whether in any other walk of life advances in salary cease so soon. My friend, Courtney Werner, has aptly said that a university professor is one who spends half his life cultivating good tastes and the other half denying them.

Coming now to employment of staff in private institutions, a marked difference from public institutions is apparent. Instead of individual salaries being known, they are secrets not to be divulged on pain of dismissal. True, some of those at the top receive better salaries than are ordinarily paid in public institutions, but those in the middle and especially near the bottom are underpaid, and very little can be done about it. There is not enough money to go around. And there is the dreadful uncertainty of the survival of private institutions in the postwar epoch. Staff members have the jitters and deans are anxious but outwardly confident for their own particular faculties. Indeed, the greatest threat to private institutions is a massive exodus of staff members. The influences promoting this exodus are not hard to find.

M. H. Trytten, of the Office of Scientific Personnel of the National Research Council, has eloquently described the lure of expanding industry. Note, as he has, that this will come at a time when the universities and colleges are least able to supply the demand, because education has been curtailed. Add to this the probability that industry will be aided by Government, and that the high scale of living somehow will be maintained except for those in non-profit private institutions of higher education, who are the forgotten ones. President Conant, of Harvard, has urged industrial laboratories not to "kill the goose that lays the golden eggs." It is not only industry in the limited sense of this term that may deplete the private institutions of their staff members, but also the increasing attractiveness of extramural employment all along the line, since universities are universal in their services.

Consider the public educational institutions with which the private ones must compete. The University of California has come forward with a \$27,000,000 building program, and others will not be far behind. A federal appropriation of \$300,000,000 to the States for education is contemplated, a large share of which will go into buildings. Increase in demand for staff will follow construction of buildings as certainly as day follows night. Where are these thousands to come from?

In 1941-42, 1,067 private universities, colleges and professional schools reported 67,706 "full time equivalent" staff members, not counting those in the summer schools. Are these to melt away? What advice can we give them, as well as thousands of returning veterans now on leave from private institutions? Security is what they seek for themselves and their families, present and future. If they are young and expect to make several moves before they settle down, public institutions have no great advantage. If, however, they are nearing the critical age of forty, employment in a tax-supported institution is more attractive.

Whereas the shift of students from private to public institutions, already referred to, will be gradual but at an increasing tempo, the shift in staff may take place quickly, massively, like a land slide, aggravating the loss to industry, and then the quality of instruction will surely deteriorate so that excuse for survival of private institutions will evaporate.

The big question is, How can federal aid properly be extended to them? They do not want federal control, and Congress is rightly averse to extension of this control, especially in education. Legislation might be enacted to provide \$100,000,000 to salvage private higher education. But how much should be given and to which institutions? A mad scramble might ensue for federal money. Control by the Fed-

eral Government inevitably would follow the dollars. This would be a disadvantage, but beggars can't be choosers. The fortunate ones would soon be back for more.

An alternative would be to adopt the pound-per-pound plan which has been successful in the Union of South Africa or some modification of it, whereby the Federal Government would match dollar for dollar certain voluntary gifts to private institutions. Though this, unlike outright aid, would definitely encourage wealthy citizens to give at a time when the Government seems bent on their suppression, administrative difficulties would be legion. For a bureau in Washington to decide which gift to which institution should be matched and which should not would be an embarrassing task. It would bring a steady stream of supplicants to the nation's capital, generate much hard feeling, and Congressmen and Senators continually would be worried by the folks at home.

But there is a way by which financial aid can be extended without each institution having elaborately to present its case, without accompanying federal control and in such a form that it will stabilize financial structure of educational institutions and encourage them to help themselves.

If our elected representatives in Washington are agreed that private initiative in higher education must be preserved, they might well give serious consideration to a plan presented at a hearing of a Subcommittee on Health and Education (Senator Claude Pepper, *chairman*) last December.

This involves the issuance of a special series of 5 per cent. Government bonds, purchasable only by these non-profit institutions of higher education up to a certain fraction of their endowment, as recorded in the U. S. Office of Education. The bonds would be non-transferable and have a life of about 25 years. It is questionable how much each institution should be permitted to buy. To make this a fraction, say one half, of their endowments on record in the U. S. Office of Education would be simple; but it would give the greatest relief to those with the largest endowments.

An apparently fairer method would be to base the privilege of buying such bonds on the volume of educational service rendered during 1940, the last normal year in this country. A formula could easily be devised which would give an index purchase figure for each institution taking into consideration not only the total number of students enrolled but also the percentages of students who were part-time in summer or night school, full-time in regular courses and post-graduates. Since the educational service rendered per student in these and other categories is not the same under all conditions, it would be obviously unjusti-

fiable to allow two institutions having the same total enrolment to purchase equally unless their index purchase figures were the same.

Suppose that \$750,000,000 in federal securities were to be purchased, the Government paying 5 per cent. would be giving about 3 per cent. above the usual rate of say 2 per cent. It would, therefore, be granting without fear or favor an actual subsidy of \$22,500,000 per annum, or 3 per cent. of \$750,000,000. The amount is small in comparison with the issue at stake. In the event of a specified general and sustained rise in rate of interest on investments, the subsidy would no longer be needed and a provision in the bonds to cover this contingency might go into effect so that they would be retired by the Government.

It is easy to think of objections to this or any other plan of salvage and to use them as excuses for doing nothing. One objection is that it would help the strong as well as the weak, and some institutions which are perhaps not worthy. But private higher education is a great non-profit industry of value to the nation, which as a whole requires a transfusion without invidious distinction as to its parts.

Some persons have expressed doubt as to the legality of such legislation. To these I quote the following from an opinion kindly rendered by Mr. Elmer E. Hilpert, professor of constitutional law in Washington University, which reads in part as follows:

It is clear that the proposed scheme would not exceed the delegated powers of Congress. Congressional power to spend to promote the general welfare is not limited to the narrow range of purposes with respect to which Congress has power to regulate. Under its power to spend for the general welfare the federal government supports a variety of activities in fields in which it has no power to regulate. Among these is the Office of Education. Hence, the promotion of collegiate and university education is clearly within the analogies of federal expenditures that have been sustained.

Nor would the expenditure of federal tax receipts to pay the proposed "advantageous" interest rates violate the due process clause of the constitution. It is true that public money may not be diverted to private purposes within the meaning of the due process clause. But every aid to a private person or institution is for a purely private purpose. There are many instances where public aid to private institutions can be, and has been, sustained as sufficiently serving a great purpose to meet the test of the due process clause. It is hard to conceive of the Supreme Court's failing to recognize that public aid to private colleges and universities is closely related to the development of a trained personnel essential to a nation's welfare, both in peace and in war.

Neither does the proposed scheme constitute an establishment of religion in violation of the First Amendment, even if its benefits are extended to so-called sectarian institutions. Such governmental support would not

...within either the historical meaning of the term—establishment of religion—or within the reason for the constitutional rule prohibiting the establishment of religion. Realistically, sectarian colleges and universities (which exclude avowed theological seminaries) do not exist to perpetuate a religion but to provide secular education; and neither do they as a general rule restrict admission to members of the sect supporting such institution. And the preference of colleges and universities as investors in the proposed bonds would not deny equal protection of the laws to those excluded from investing therein. Not every preference in legislation is a denial of equal protection of the laws. If classification is necessary to accomplish the purposes of the legislation and if the classification is reasonably related to the accomplishment of these purposes, then, assuming the validity of the legislative purpose and objective, the legislation will not fail merely because there is such preferential or differential treatment among the body of citizens. Here the very object of the legislation is to provide advantageous investments for private colleges and universities. Conceding that such aid to private institutions sufficiently serves a public purpose to meet the requirement of due process of law, the preference of such private institutions is a necessary device to effectuate the object of the legislation. Indeed, if the requirement of equal protection of the laws were to be given a doctrinaire interpretation, the legis-

lature would find itself in a constitutional straight-jacket, for the very purpose of much legislation is to single out some public need and provide the means to meet it.

The unkind may say that this is altogether too simple a solution devoid of attractive red tape. It would not result in the growth of a large bureau, applicants would not flock to Washington, and our elected representatives there would have no opportunity to display their prowess in the support of the schools and colleges at home. It would simply be the right of all private institutions of higher education listed in the U. S. Office of Education to avail themselves of this federal aid in proportion to the educational service they perform.

The idea of issuing a special series of 5 per cent. non-transferable Government bonds is mentioned because it seems to be workable. But any plan of federal aid unaccompanied by federal control would be welcome. The time for inaction is past. It is up to these great private schools and colleges from Maine to Florida and from Washington to California and in between to get together and tell the public what they really want, for legislation may be passed almost any day, which, by supporting only public institutions, will make their survival even more precarious.

RAINFALL PERIODICITY IN RELATION TO MALARIA AND AGRICULTURE IN THE NEAR EAST

By DR. HELMUT DE TERRA

VISITING PROFESSOR OF GEOGRAPHY, THE OHIO STATE UNIVERSITY

THE literature on the Near East is full of speculative references to climatic changes as having altered the history of its peoples. Depopulation of Palestine and Syria in ancient times, shifting of caravan roads and cities, loss of soil fertility, wars between sedentary and nomadic peoples have at one time and another been related to rainfall and vegetation changes. In a most recent book by W. C. Lowdermilk¹ the problem is posed anew. In opposition to Ellsworth Huntington's² claim for climatic changes, its author suggests that soil erosion is chiefly responsible for the vanishing of wealth and power in the Near East. In other sources the evidence in favor of climatic controls frequently referred to vanishing forests, to shrinking croplands and to abandonment of elaborate water works. In the other camp are those who emphasize social factors as degeneration of farm practices, raids of desert nomads, excessive taxation and diseases like malaria. The issues have been under discussion for over two generations, but they are not merely aca-

demic. On the contrary, they have eminent practical value. If the planners in the Near and Middle East would know what to guard against and at what time adverse climatic factors might arise, it would mean the saving of many human lives and of large sums of money. Already vast projects of land reclamation are under way in Palestine. Others are scheduled and will be tried out in adjoining regions which stir afresh under the touch of reformist movements. Hence a clarification of the issues is as timely as it is desirable.

It seems to me that a new approach to this complex question can be found in analyzing observable climatic records and in relating these to one of the better-known scourges like malaria and crop failures. Rainfall of course is the most important climatic factor in these lands. Meteorologic recordings go back sufficiently in time to permit of definite conclusions as to the periodicity of rainfall and water supply. Long-range recordings are available from stations like Beirut, Haifa, Jerusalem, Gaza and others. A preliminary study of these records tends to disclose that a very real control has been exercised over the welfare

¹ "Palestine, Land of Promise." New York, 1944.

² "The Transformation of Palestine," Boston, 1911, and "Climatic Falsations," Hyllningskrift Sven Hedin, Stockholm, 1935.

of those lands for the last thirty years by observable minor climatic variations.

The accompanying rainfall graphs (Fig. 1) represent a period of sixty-six years. The data were taken from government sources as well as from H. H. Clayton's "World Weather Records."³ These graphs disclose the following tendencies. A rainfall periodicity making for alternate wet and dry "phases" with rainfall maxima corresponding roughly with sunspot maxima. Years with excessive rainfall tend to recur in phases of 10 to 12 years, namely, 1883 to 1893, 1893 to 1906, 1906 to 1917, 1917 to 1929 to 1938. Wet and dry phases have their own oscillations which run counter to their respective tendencies. This introduces a non-periodic element which is presumably due to local storms. The single phase appears to swing away from the total average rainfall by three and four inches, e.g., a rainy phase shows an aggregate surplus of four inches over and above the general mean (Beirut: 35.2 inches). Years with excessive rainfall within a wet phase show increases of 30 to 50 per cent. of the general rainfall mean and up to 70 per cent. from one rainy season to another. The rainfall curves also indicate a secular change as revealed by a slight downward trend toward aridity. Whether this is in the nature of a cyclic process or whether it is a one-way change cannot be determined.

Significant also is that excessively wet years are preceded by one or two dry years. This means that after a drought season streams have to remove unusual quantities of weathered rock with resultant overloading and widespread ponding. In such rainy years lakes and open reservoirs experience a sudden expansion, forming additional breeding grounds for malaria mosquitoes. This is especially true for the dry wadis and for the coastal dune belt, where successive dune ridges accompany the shore through which the streams must cut in order to reach the Mediterranean. On the inland plains such rains lead to flooding of valley floors and the formation of stagnant pools. At such times climatic optimum conditions prevail for a malaria epidemic.

To substantiate and clarify this relationship it should be remembered that it was the late malariologist, Dr. I. J. Kligler,⁴ formerly of the Rockefeller Institute, who demonstrated that in Palestine malaria spreads with the seasonal rhythm of rainfall and air temperature. There the rainy seasons last from October to April while the summers are dry and hot. It is in the spring that cisterns, ponds and lakes are filled with water and that stagnant pools occur in

the valleys. These are the ideal breeding grounds for the malaria hosts. Since the rainy season generally will come to an end in April and with air temperature rising from then on, larvae of the malaria-carrying mosquitoes will mature quickly. The malaria parasites in their mosquito hosts will complete the regenerative cycle within a month. This means that in May mosquitoes begin to play their deadly role on malaria hosts. From then on the percentage of malaria infections rises steeply until an optimum is reached in June and July. In August begins a waning which lasts until November when rains and low temperatures cause a "dormant phase." This generally lasts until the following spring. According to Kligler's careful studies this seasonal rhythm is found in the coastal plains where the mosquito hosts become active twice. In the inland plains, however, the malaria optimum is reached in the fall occasioned by later activity of a different species and at a time of greater humidity. Kligler's observations were carried out over a period of two and a half years (1924-1926) and his graphs indicate a rapid rise of malaria infections at the end of 1926. This epidemic coincides with one of the prominent wet phases in Fig. 1.

This striking relationship between rainfall maximum and malaria epidemic is confirmed by records of previous epidemics in the Near East. The calamitous epidemic of 1917-19 which struck Syria, Transjordan and Palestine is well known. It had been suspected that this outbreak was due to an unusual influx of malaria carriers through Turkish and Allied troop movements from countries further east and southeast. However, this outbreak was not confined to these regions but it also affected areas like Greece and the Balkan countries where relatively fewer malaria carriers of eastern origin were stationed during the war. Hence it would seem more plausible to relate this epidemic to the excessively wet phase that prevailed during these years, especially since those countries have similar rainfall régimes (Fig. 1). Preceding it, in the years 1911-1912, Brunn and Goldberg⁵ recorded an unusually high percentage of malaria in the Judean Hills. This also was a time of abnormally high rainfall (Fig. 1). Still earlier Dr. John Cropper (*Journal of Hygiene*, V, 1905) found a high rate of infections for the years 1904-05 in Jerusalem. Again this corresponds with the wet phase recorded in Fig. 1.

That the waning of the great epidemic of 1917-19 could not be attributed solely to anti-malarial measures was plainly admitted by the Malaria Commission of the League of Nations.⁶ The question con-

³ "Die Malaria Jerusalems und ihre Bekämpfung," *Zeitschrift für Hygiene*, Vol. 75.

⁶ "Reports on the Tour of Investigation in Palestine in 1925," League of Nations Health Commission, Geneva, 1925.

³ I wish to acknowledge with sincere thanks the assistance of Lloyd Stevens, acting director, Statistics Division, U. S. Weather Bureau, who furnished me with certain data.

⁴ "The Epidemiology and Control of Malaria in Palestine," Chicago University Press, 1930.

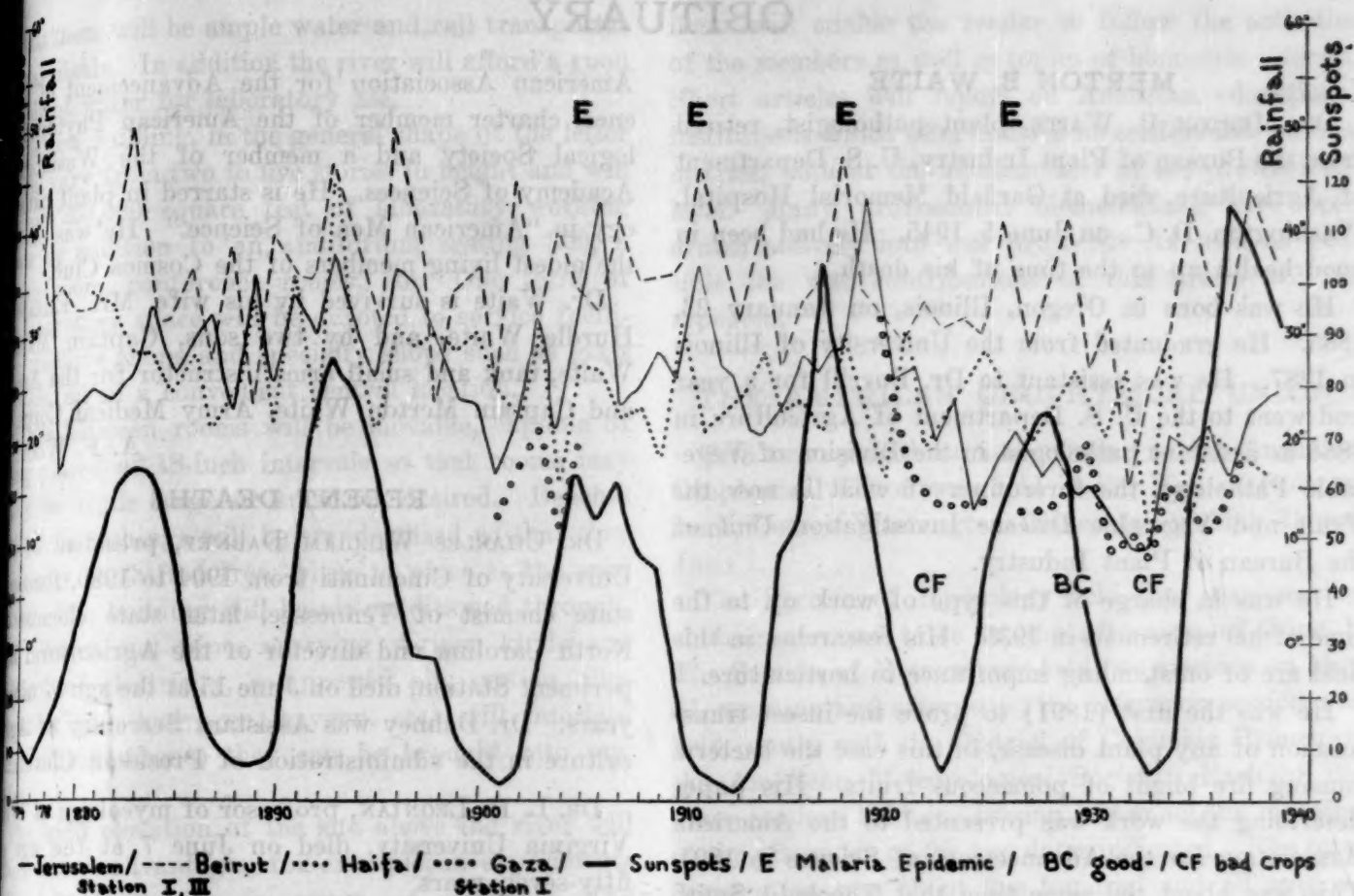


FIG. 1

erning the controlling factor of malaria epidemics in the Near East was thus left unanswered.

Theoretically speaking, a climatic control of malaria epidemiology in the Near East may work out differently if we admit that any abnormality of rainfall can produce social stress conditions in marginal lands. Excessive drought, for instance, frequently forces desert dwellers to overrun the adjoining farm-lands in their search for food resources. If this drought is followed by a rainy phase, a malaria optimum will be reached, by both a sudden influx of malaria carriers and rapid expansion of breeding grounds. No data are available to me to indicate that such an epidemic was caused ever by a drought. In any event such a contributing factor can hardly be called social when it is induced by climatic processes which cause the burning up of croplands or pastures in times of drought.

This latter aspect leads to another relationship concerning the impact of wet and dry climatic phases upon food crops in the Near East. Sufficient data are already at hand to prove that bumper crops of wheat and barley, the chief staple farm products, coincide with wet phases and conversely crop failures with dry phases. The data submitted on the graph are based on statistics from Syria and Palestine. This, as well as other aspects, will be more fully described on another occasion.

The climatic agencies which produce these rainfall

changes would seem to be influenced by the sunspot cycle, yet it remains to be seen how exactly this relationship works in terms of atmospheric circulation. It has been suggested to me by H. Bowman Hawkes, of the Department of Geography at Ohio State University, that the alternate phases might be induced by a periodic shifting of the cyclonic storm tracts in the Eastern Mediterranean. This will require a special study which is at present under way.

Once more it becomes apparent that the study of climatic changes and their impact on human society must rely on demonstrable observations rather than on inferences drawn from historic records. Of all other approaches, the geographic method lends itself better to a full elucidation of these inter-related processes because it can synthesize what would otherwise remain unrelated to observable facts. In this case it would seem that rainfall periodicity once recognized and substantiated by more data may actually lead to the prediction of conditions conducive to epidemics and crop failures. In this manner it may be possible not only to undertake preventative measures but to understand more clearly the relationship between climate and human planning. And if, as in this case, the relationship could be fully understood on the basis of observable records, I can see no objection to an acceptance of Huntington's theory whereby the historic fate of Near Eastern nations has at certain times been greatly affected by changes of climate.

OBITUARY

MERTON B. WAITE

DR. MERTON B. WAITE, plant pathologist, retired from the Bureau of Plant Industry, U. S. Department of Agriculture, died at Garfield Memorial Hospital, Washington, D. C., on June 5, 1945. He had been in good health up to the time of his death.

He was born in Oregon, Illinois, on January 23, 1865. He graduated from the University of Illinois in 1887. He was assistant to Dr. Burrill for a year and went to the U. S. Department of Agriculture in 1888 as assistant pathologist in the Division of Vegetable Pathology, the forerunner of what is now the Fruit and Vegetable Disease Investigation Unit of the Bureau of Plant Industry.

He was in charge of this type of work up to the time of his retirement in 1935. His researches in this field are of outstanding importance to horticulture.

He was the first (1891) to prove the insect transmission of any plant disease, in this case the bacteria causing fire blight of pomaceous fruits. His paper describing the work was presented to the American Association for the Advancement of Science in 1891. This was about the same time that Theobald Smith and associates, 1891, proved the transmission of tick fever of cattle. These were the first demonstrations of insect or tick transmission of plant and animal diseases. These two pioneer demonstrations led to the work which proved that malaria and yellow fever were carried by mosquitoes and to the beginning of control of these and similar diseases. His work on cross pollination of fruit varieties led to the successful production of orchard crops of apple, pear, sweet cherry and other fruits.

Dr. Waite was lecturer on plant diseases in the Graduate School of the Department of Agriculture from 1930 to 1938 and lecturer on plant ecology from 1932 to 1938.

He was awarded the honorary degree of doctor of agriculture by the University of Maryland in 1919. He was a charter member and twice president of the Botanical Society of Washington, fellow of the

American Association for the Advancement of Science, charter member of the American Phytopathological Society and a member of the Washington Academy of Sciences. He is starred in plant pathology in "American Men of Science." He was one of the oldest living members of the Cosmos Club.

Dr. Waite is survived by his wife, Mrs. Elizabeth Hurdle Waite, and by two sons, Captain Malcolm Waite, tank and small arms instructor for the Army and Captain Merton Waite, Army Medical Corps.

A. F. Woods

RECENT DEATHS

DR. CHARLES WILLIAM DABNEY, president of University of Cincinnati from 1904 to 1920, former state chemist of Tennessee, later state chemist North Carolina and director of the Agricultural Experiment Station, died on June 15 at the age of ninety years. Dr. Dabney was Assistant Secretary of Agriculture in the administration of President Cleveland.

DR. L. H. LEONIAN, professor of mycology at Washington University, died on June 7 at the age of fifty-seven years.

RICHARD S. MCCAFFERY, mining engineer, who was professor of mining and metallurgy at the University of Wisconsin from 1914 to 1941, died in New York City on June 13 at the age of seventy-one years.

CHARLES ERNEST PELLEW, Viscount of Exmouth and assistant professor of chemistry at Columbia University, died on June 7 at the age of eighty-two years.

THE death on June 2 at the age of seventy-nine years is announced of Dr. Shim Shirayama, professor emeritus of astronomy of Tokyo Imperial University, a member of the Imperial Academy.

IN the announcement sent to SCIENCE of the death in Yugoslavia of Lieutenant Wheeler, formerly of Harvard University, it was stated that he was assistant professor. This is incorrect. His title should have been given as associate professor.

SCIENTIFIC EVENTS

PLANS OF THE GENERAL ELECTRIC COMPANY FOR A NEW RESEARCH LABORATORY

A NEW building for the General Electric Company's Research Laboratory, which will afford some fifty per cent. more space than present facilities provide, will be erected at a cost of \$8,000,000 near Schenectady, N. Y. Construction will begin as soon as WPB approval can be obtained.

The site has been a private estate known as "The Knolls," and includes 219 acres. It is in suburban Niskayuna, about four and a half miles from the main plant and offices in Schenectady. Overlooking the Mohawk River, it is on a rocky cliff which will afford an excellent and solid foundation for the laboratory buildings. The river at this point forms part of the New York State Barge Canal, and the Troy branch of the New York Central runs along the bank.

that there will be ample water and rail transportation available. In addition the river will afford a good supply of water for laboratory use.

The new building, in the general shape of the letter 'E', will vary from two to five stories in height and will include 200,000 square feet of laboratory working space in addition to an auditorium seating 300, a dining room, conference rooms, etc. One third of the laboratory space will be devoted to service facilities, machine shops and specialty shops such as glass blowers, all in a convenient central location.

Walls between rooms will be movable, capable of being placed at 18-inch intervals so that rooms may easily be made large or small as desired. Benches and all furnishings will be standardized so that they can easily be shifted from place to place as the need arises. The building will be air-conditioned throughout.

Wires and pipes carrying various kinds and voltages of electricity, compressed air, suction, illuminating gas, hydrogen, oxygen, etc., will interlace the building whence they can be brought into any room.

The high elevation of the site above the river will afford many advantages, for example, in experiments with radar and high frequency jet engines. The rocky cliff foundation will be useful in conducting experiments with x-rays. These are being produced at a hundred million volts in the present laboratory, and further increases are expected.

THE BIOMETRIC BULLETIN

The Biometrics Section of the American Statistical Association has issued the first number of the *Biometric Bulletin*, which it is planned to issue monthly. According to the official statement, the *Bulletin* will be developed to meet the needs of the membership of the association. Many features have been planned primarily for the novice. There will be a column of queries to which members are invited to submit questions which can be answered briefly. Questions concerning statistics, for example, can be answered here authoritatively.

Larger problems will be covered by short expository articles written on invitation by qualified professional biometricians. Review articles will emphasize the applications of statistics in substantive fields such as geology, entomology, forestry, plant breeding, bacteriology and many others. The first of these, on uses of statistics in medicine, appears in the first issue. Although few of the papers read at the meetings of the section can be published in full, abstracts of them, usually in advance of their final publication, will appear.

The section will continue to hold joint meetings with biological as well as with statistical societies, and the *Bulletin* will carry notices of these programs. News

items will enable the reader to follow the activities of the members as well as topics of biometric interest. Short articles will report on American educational institutions which offer courses or conferences on biometrics, both at the amateur and at the professional level. Many professional biometricians have been drawn actively into war projects. As soon as possible the war contributions of this group will be reported.

THE AMERICAN GEOPHYSICAL UNION

The twenty-sixth annual meeting of the American Geophysical Union was held in the Hall of Government, George Washington University, on May 31 and June 1.

The Section of Hydrology held four sessions, including a round table on the afternoon of June 1. The Section of Meteorology held two sessions on May 31, morning and afternoon; the afternoon session was held jointly with the District of Columbia Branch of the American Meteorological Society. Each of the other sections held one session, either on the morning or the afternoon of the two dates indicated. The total registration was about five hundred and all sessions were very well attended.

The session of the Section of Terrestrial Magnetism and Electricity attracted especially large attendance on the morning of May 31. On the afternoon of May 31 the session of the Section of Volcanology attracted a large group. Among the interesting features of this meeting was the showing of the moving picture of the Volcano Parícutin. Some of the other papers presented at this same session bore on the same subject and included a number of interesting slides. At all the sessions eighty-seven papers and twelve Research Committee reports were given or read by title.

The business session was held on the afternoon of June 1, at which seven resolutions were passed. The seventh award of the William Bowie Medal was made in absentia to Dr. Jacob A. B. Bjerknes, chairman of the department of meteorology, University of California at Los Angeles.

Leonard M. Murphy, of the U. S. Coast and Geodetic Survey, was elected secretary of the Section of Seismology. No other elections were held.

Announcement was made concerning the last will and testament of the late Dr. Robert E. Horton, of Voorheesville, New York. Under this will, much of the residual estate will ultimately be given to the National Research Council for use by the American Geophysical Union in the furtherance of research in hydrology.

The executive committee of the union held a meeting on the afternoon of June 1, immediately following the business meeting of the union.

THE AMERICAN ASTRONOMICAL SOCIETY

THE annual business meeting of the American Astronomical Society was held at the Harvard Observatory on June 8. The general meeting was preceded by a dinner meeting of the council at the Harvard Faculty Club.

Owing to restrictions on conventions, the meeting was of local character and no scientific program was attempted. Members cast their ballots for the election of officers by mail. The number of members who attended in person was thirty-nine, of whom seven were members of the council. Only four persons traveled more than a hundred miles, and three of these were councilors.

New officers of the society were elected as follows:

- Vice-president*, 1945-1947, Alfred H. Joy, Mount Wilson Observatory
Secretary, 1945-1946, Dean B. McLaughlin, University of Michigan
Treasurer, 1945-1946, Keivin Burns, Allegheny Observatory
Councilors, 1945-1948, N. T. Bobrovnikoff, Perkins Observatory
 A. D. Maxwell, University of Michigan
 R. M. Petrie, Dominion Astrophysical Observatory

Officers who continue unexpired terms are as follows:

- President*, 1943-1946, Harlow Shapley, Harvard Observatory
Vice-president, 1944-1946, J. A. Pearce, Dominion Astrophysical Observatory
Councilors, 1943-1946, Harold D. Babcock, Mount Wilson Observatory
 1943-1946, Dirk Brouwer, Yale University Observatory
 1943-1946, J. J. Nassau, Case School
 1944-1947, N. U. Mayall, Lick Observatory
 1944-1947, Peter Van de Kamp, Swarthmore
 1944-1947, John S. Hall, Massachusetts Institute of Technology
Ex-presidents, 1940-1946, R. G. Aitken, University of California
 1943-1949, Joel Stebbins, University of Wisconsin

A nominating committee was elected as follows: Joel Stebbins, *Chairman*; B. J. Bok, Dirk Brouwer. It is the duty of this committee to prepare the list of candidates for the next election of officers, which will take place at the annual business meeting of the society in 1946.

Certain special actions of the council will be announced to the membership at a later date.

DEAN B. McLAUGHLIN,
Secretary

HONORARY DEGREES CONFERRED BY COLUMBIA UNIVERSITY

As reported last week in SCIENCE Dr. Edwin Joseph Cohn, of Harvard University, and Dr. Herbert Spencer Gasser, director of the Rockefeller Institute for Medical Research, received the degree of Doctor of Science at the one hundred and ninety-first commencement of Columbia University on June 5. The citations made by Dr. Nicholas Murray Butler, president of the university, in conferring the degrees follow:

EDWIN JOSEPH COHN:

Professor of biological chemistry in the Medical School of Harvard University; student at Amherst College who later received the degrees of Bachelor of Science and Doctor of Philosophy from the University of Chicago; then pursued advanced studies in his chosen field of physical chemistry of proteins at Carlsberg Laboratory in Copenhagen and Cambridge University; now engaged in productive research in the physiology and chemical composition of the blood, the results of which have not only greatly increased fundamental scientific knowledge but have saved many thousands of lives among those wounded in the war.

HERBERT SPENCER GASSER:

Director of Rockefeller Institute; received the degrees of Bachelor of Arts, Master of Arts and Doctor of Science from the University of Wisconsin and that of Doctor of Medicine from Johns Hopkins University; since 1935 director of the Rockefeller Institute; awarded in 1944 the Nobel Prize for work in medicine and physiology; outstanding in the organization and conduct of scientific research in his chosen field of physiology of the nervous system; constantly making important contribution to the understanding of the mechanisms of the nerve impulse and its action in the human body.

SCIENTIFIC NOTES AND NEWS

WILLIAM FONDILLER, assistant vice-president of the Bell Telephone Laboratories, was awarded on June 5 the University Medal at the commencement exercises of Columbia University in recognition of "his important contribution to the development of the telephone."

THE Eli Lilly and Company Award in Bacteriology and Immunology for 1945 was conferred on May 26 at Austin, Texas, on Dr. Esmond E. Snell, a member of the research staff of the Clayton Biochemical Institute of the University of Texas. The award, which consists of a check for one thousand dollars and a

...ably engraved medal, was presented to Dr. Snell in recognition of his "outstanding contributions to our knowledge of the intimate nutritional requirements of microorganisms." Selection of the recipient of the award is made by committees of the Society of American Bacteriologists, the American Association of Immunologists and the American Society for Experimental Pathology. The Eli Lilly and Company has made an additional grant making possible three more awards, presumably for 1946, 1947 and 1948.

PROFESSOR RICHARD STEVENS BURLINGTON, of the Case School of Applied Science, director and organizer of a research analysis group in the Research and Development Division of the Bureau of Ordnance, has received the Meritorious Civilian Service Award of the U. S. Navy. His work is in the field of mathematical and physical analysis, and in research connected with ordnance problems. The citation, presented by Admiral G. F. Hussey, chief of the Bureau of Ordnance, reads: "For meritorious civilian services to the U. S. Navy. As a contract employee attached to the Underwater Ordnance Section of the Research and Development Division, he has constantly and consistently concerned himself with aspects of the anti-submarine program which are considerably in excess of his required duties and has at the same time developed unique methods and procedures for evaluation of anti-submarine weapons, the net result of which has been to provide this Bureau and the Commander-in-chief, U. S. Fleet, with information and analyses which have resulted in savings of material, time and manpower that would otherwise have been expended in pursuit of less valuable experimental and development programs."

WILLIAM ILER BEACH, chief plastic engineer of the North American Aviation, Inc., at Inglewood, Calif., has been presented with the fourth annual John Wesley Hyatt Award, carrying with it a gold medal and \$1,000, in recognition of his work in "designing plastic airplane parts that saved weight and manufacturing time in fighting planes." The John Wesley Hyatt Award was established in 1941 by the Hercules Powder Company to honor the founder of the plastics industry, who invented celluloid in 1867.

IN anticipation of his retirement on September 1, 1945, Dr. Percy E. Raymond, professor of invertebrate paleontology at Harvard University, was tendered a dinner on June 7 by sixty-four of his colleagues, former students and friends. Professor Carl D. Dunbar, of Yale University, gave the principal address on "Raymond—the Paleontologist." A book of letters, written by ninety-four colleagues and former students and a pewter tankard were presented to Professor Raymond. Also, in recognition of his emi-

nence in the field of collecting, Charles H. Watkins spoke on his services to the Pewter Club of America.

THE honorary doctorate of science of Alfred University was conferred at the commencement exercises on Dr. Heinrich Ries, professor emeritus of geology at Columbia University, "in recognition of a lifetime of devotion service in writing, teaching and organization and research in the twin fields of ceramics and geology."

NORTHEASTERN UNIVERSITY conferred on June 3 on Professor C. L. Dawes the honorary degree of doctor of engineering. The citation by Dr. Carl Stephens Ell, president of the university, was as follows: "Because, as a prominent electrical engineer, your work has been characterized by much significant research and scholarly production and also by a high degree of efficiency as a consulting engineer and because of your contribution to the development of high standards of engineering education through the United States, the Board of Trustees have authorized me to confer upon you the honorary degree of Doctor of Engineering."

DR. EDWARD A. MILNE, Rouse Ball professor of astronomy at the University of Oxford, who was awarded the Catherine Wolfe Bruce Gold Medal of the Astronomical Society of the Pacific for the year 1945 in recognition of "distinguished services to astronomy," was formally presented with the medal at a meeting of the Royal Astronomical Society in London on May 11. The presentation ceremony was conducted by Sir H. Spencer Jones, F.R.S., Astronomer Royal.

DR. VICTOR F. CULLEN, superintendent of the Maryland State Sanatorium, has been elected president for 1946 of the National Tuberculosis Association. He will succeed Dr. Will Ross, of Milwaukee, who assumed office on June 8.

THE Institute of Food Technologists has elected Dr. F. W. Tanner, head of the department of bacteriology of the University of Illinois, president, and Dr. Victor Conquest, director of research and development, Armour and Company, Chicago, vice-president.

THE retirement is announced at the Medical School of the University of Wisconsin of Dr. Charles H. Bunting, professor of pathology, and of Dr. Joseph S. Evans, professor of medicine.

DR. CHARLES J. MOORE, since 1921 professor of chemistry at Hunter College, New York City, will retire in September.

DR. PAUL F. GAEHR, professor of physics at Wells College, is retiring after having served for thirty-

four years. He will be succeeded by Mrs. Charlotte Houtermanns.

At the Ohio State University, members of the faculty having reached the university retirement age are Professor Charles C. Morris, since 1908 a member of the department of mathematics; Professor Charles Scott Berry, since 1930 director of the Bureau of Special and Adult Education, and Professor Oscar Erf, since 1907 a member of the staff in animal husbandry and agricultural extension. Those exercising the privilege of voluntary retirement include Professor William M. Barrows, since 1909 a member of the department of zoology; Dean Arthur J. Klein, since 1937 dean of the College of Education, and Professor Raymond J. Seymour, since 1904 a member of the department of physiology.

DR. ROLF C. SYVERTSEN, professor of anatomy at Dartmouth College, has been appointed dean of the School of Medicine, effective on July 1. Dr. Syvertsen, who has for many years been secretary of the school, succeeds Dr. John P. Bowler, who has resigned but who will continue as a member of the medical faculty as professor of surgery.

RESEARCH professors at the University of Missouri have been appointed as follows: Leonard M. Blumenthal, mathematics; Douglas R. Hansen, fine arts; Walter D. Keller, geology; Jacob Levitt, botany, and Lloyd E. Thomas, biochemistry. They will devote full time to research projects which have been approved by the University Research Council. Remuneration for the summer session will be on the same financial basis as for full-time teaching during the summer session. It is stated that this experiment in encouraging research at the university is intended to free members of the faculty from the necessity of teaching during the summer session and to make it possible for them to give undivided attention to research work. Some of them have not been on the faculty long enough to be eligible for sabbatical leave or for other reasons are not able to take advantage of this opportunity for research. These summer appointments, it is hoped, will accomplish much the same results although for a more limited period of time.

DR. LOREN C. EISELEY, professor and head of the department of sociology of Oberlin College, has been appointed visiting professor in the department of anthropology at the University of Pennsylvania during the summer session beginning on July 1. He will offer courses in primitive art, ethnology, race and culture.

F. J. REITHEL, formerly instructor in biochemistry at the School of Medicine of St. Louis University, has become associated with the Kerekhoff Laboratories of the California Institute of Technology, Pasadena.

DR. JAMES OLMSTED, professor of physiology at the University of California at Berkeley, has been appointed Hideyo Noguchi Visiting Lecturer at the Institute of the History of Medicine at the Johns Hopkins University. The subject of the lectures, to be given next spring, will be "The Life and Work of Brown-Sequard."

MAJOR F. W. SHOTTEN has been appointed Sorby professor of zoology at the University of Sheffield to succeed Professor William George Fearnside, F.R.S. who has retired after serving since 1913.

DR. W. J. HAMILTON, professor of anatomy at the University of London, has been appointed Reginald professor of anatomy at the University of Glasgow.

DR. JOSEPH C. BEQUAERT has been appointed head curator of recent insects at the Museum of Comparative Zoology of Harvard College.

DR. SIDNEY ROBERTS and Dr. Clara M. Szego, formerly instructors in the department of physiology of the Medical School of the University of Minnesota, and Dr. Min-Chueh Chang, of the University of Cambridge, have joined, as associate members, the staff of the Worcester Foundation for Experimental Biology.

CHARLES G. DANFORTH has resigned as instructor in zoology and biology at the Michigan State College to become executive biologist with the General Biological Supply House of Chicago.

DR. EDMUND VINCENT COWDRY, director of research at the Barnard Free Skin and Cancer Hospital, St. Louis, Mo., and professor of anatomy at Washington University, delivered on May 24 the first annual Charles Sumner Lecture of the Medico-Chirurgical Society of the District of Columbia. He spoke on "The Present Status of the Problem of Cancer."

DR. HOWARD T. KARSNER, professor of pathology and director of the Institute of Pathology of the School of Medicine of Western Reserve University, made an address before the Los Angeles Academy of Medicine on May 11 entitled "Tumors of the Endocrine Glands."

THE seventh annual conference of the New England Association of Chemistry Teachers of the Massachusetts State College, Amherst, will be held from August 9 to 13.

DR. S. R. BRUESCH, assistant professor of anatomy at the College of Medicine of the University of Tennessee, has leave of absence to work with Dr. Curt P. Richter at the Psychobiological Laboratory of the Phipps Psychiatric Institute of the Johns Hopkins Hospital. Dr. James O. Brown, associate professor of anatomy and acting head of the department of

anatomy of the Woman's Medical College of Pennsylvania, will be visiting associate professor of anatomy at the University of Tennessee College of Medicine for the summer quarter.

The French Press and Information Service reports that for the first time since 1940 weather forecasts are being broadcast in France. As of April 1, a network of ninety-seven observatories of the French National Bureau of Meteorology have resumed activity, while the main office in Paris has inaugurated a training

program for technicians and is planning an efficient system of weather information for postwar intercontinental airlines. In 1940 the staff of the Meteorological Bureau fled to the unoccupied zone, hoping to save their instruments and apparatus from the Germans. Although two observation boats were seized and dismantled, the members of the staff salvaged enough equipment to enable its weathermen to collect and furnish data to the Resistance. In November, 1942, when the Germans occupied the whole of France, they again managed to escape with their instruments.

DISCUSSION

WORLD STANDARD AND UNIT FOR PENICILLIN

In the inter-war period the permanent commission on biological standardization of the health organization of the League of Nations established a series of biological standards which have been widely adopted for international use. Over thirty in number, the series includes standards for antitoxins, vitamins, arsphenamines, insulin, pituitary extract and the sex hormones. It is universally acknowledged that, by their adoption and use, system and order has been introduced where chaos might easily have ensued, and that the common interests of research worker, large-scale manufacturer, administrator, physician and—most of all—patient have been safeguarded and advanced by this action taken by the commission on behalf of them all.

The rapid development of penicillin, discovered by the British professors Fleming and Florey, whether in regard to production, standardization or clinical application, raised to a position of supreme importance and urgency the necessity of establishing a common standard, and of defining a unit in terms of that standard, and so providing the means of expressing the potency of penicillin preparations in a uniform and generally accepted system of unit notation, in whatever country penicillin may be prepared and used.

All past experience has shown that, given this common standard and unit for a drug or medicament, the results of research, clinical application, production and assay, wherever these are obtained, become easily and readily comparable.

With the outbreak of World War II and consequent cessation of the normal activities of the permanent commission on biological standardization, it seemed at first as if a decision as to the adoption of a uniform standard and unit would either have to be deferred or made by representatives of Britain and the United States alone, as it was difficult for representatives of other countries to meet and confer; and, moreover,

it was only in these countries that the opportunity for extensive studies on the production, standardization and clinical application of penicillin had been provided on any considerable scale. Fortunately, it was found possible to enlist the help of Dr. R. Gautier, officer in charge of the health service of the League of Nations, with the result that a conference was held at the apartments of the Royal Society, in London, in October, 1944, under the auspices of the League's permanent standards commission, and attended by delegates from the United States, France, Canada, Australia and Britain, as well as by a number of technical observers from these countries and from South Africa and India.

Thus, although it was not possible, partly through difficulties of travel and transportation created by the war, and partly through the short notice at which the conference had to be held, to secure the attendance of representatives of many other important countries, yet this conference was as international as the circumstances of the time permitted; and there is no doubt that the decisions reached will secure world-wide recognition and adoption.

The conference was presided over by Sir Henry Dale, president of the Royal Society, who has been a member of the permanent standards commission since its inception; and Sir Pereival Hartley, director of the Medical Research Council's department of biological standards and custodian, on behalf of the League of Nations, of the international standards established by its permanent standards commission, was scientific secretary of the conference.

This body of representatives from different countries had to review the evidence submitted with a view to making decisions and reaching agreement regarding the establishment of an international standard and unit for penicillin. The conference recommended that a quantity of pure penicillin sodium salt, provided for the purpose by manufacturers in the United States and Britain, be adopted as international standard; and that it be kept, under conditions ensuring its safety and permanence, at the National Institute for Med-

ical Research, London, from which center it shall be supplied to the directors of national control centers in other countries.

The conference also recommended that an international penicillin working standard, consisting of a calcium salt of penicillin, shall be established and made available for general distribution. This is to be held at the London Institute and distributed to all who may require it in any country in the world.

The conference recommended that the international unit should be defined as the specific penicillin activity contained in 0.6 microgram of the international penicillin standard defined above, and that 2.7 micrograms of the present international penicillin working standard be accepted as containing 1 international unit of penicillin.

These recommendations, recording agreement reached by a representative body of scientific experts reviewing all the available evidence, mark an important stage in the development of this remarkable medicament. It may be noted that the international unit recommended for adoption by the conference is approximately equivalent to the unit originally adopted by Heatley and Florey and commonly known as the "Oxford" unit.

It was also gratifying to find, by a study of the results of assays of the same samples of penicillin carried out in Europe and North America, that practically the same potency values were obtained in all the laboratories; not only does this indicate that reliable and easily applicable methods of assay are available, but the results also show that, in this interim period pending the establishment of an international standard, the temporary standards adopted on both sides of the Atlantic were closely similar.

With the establishment of an international standard the possibility of units of different value being used in different countries, and the inevitable resulting confusion, has ceased to be a matter of anxiety. Henceforth, workers throughout the world will use the same basis of dosage; they will mean exactly the same thing when they speak of a unit of penicillin, and the results obtained in one laboratory or clinic will be comparable with those obtained in other centers, whether in the same or other countries.

The material results of the conference are important, and their effect on many penicillin problems will be immediate and enduring. On more general grounds, too, this meeting of experts was an important occasion. The standards established by the commission have been made available from the department of biological standards to all accessible countries during the war, and, moreover, some new standards have been established and provided, and the work of the commission has been kept going throughout these troubled times.

It is a good augury for the future of international cooperation in scientific and medical research that even in times like these, a conference with some claim to being international can be assembled; and that by friendly discussion and frank expression of individual views decisions can be reached and agreements freely negotiated to the lasting benefit and the advancement of the best interests of all the peoples of the world.

PERCIVAL HARTLEY,

Director of Biological Standards,
British Medical Research Council

AZIMUTHAL EQUIDISTANT MAP

THE article on "An 'Air Age' Map of the World" contains a misconception about map projections. It is stated that "on the azimuthal equidistant map a straight line indicates a Great Circle course." This is true only of great circles passing through the center of the map; all other great circles appear on the map as curves concave toward the center of the map. For example, the locus of points distant 90 degrees from the center of the map is a great circle, but it appears on the map as a circle.

The characteristics of an azimuthal equidistant map are that all great circles passing through the center of the map are straight lines; the azimuths of all points with respect to the center are correctly shown; and all distances from the center are correctly shown. It is valuable for planning flights from the point with respect to which it was constructed, but is inferior to many other maps with respect to any other point.

For example, there is actually one projection on which all great circles become straight lines, namely, the gnomonic. To secure this feature, it distorts shapes at even moderate distances from the center.

H. HERBERT HOWE

ARLINGTON, VA.

BOTANICAL WORK OF THE CINCHONA MISSIONS

THE issue of SCIENCE for February 16 (Vol. 101, No. 2616), just arrived here, includes on page 177 a report on "The Botanical Work of the Cinchona Missions in South America" by Dr. Wm. C. Steere, of the University of Michigan. Although the title indicates clearly that the article is concerned with the botanical aspects of the cinchona missions, the report includes statements which make it easy to infer that the botanists alone were responsible for the success of the missions. Specifically, reference is made to the seventh sentence in the second paragraph, the first sentence in the last paragraph and the last sentence in the third paragraph, which starts out "Consequently, the great volume of cinchona bark resulting from our work," etc. Before that sentence

¹ SCIENCE, 101: 425, 1945.

the botanists had been mentioned. Later, he give high praise to the chemists, but he makes mention whatever of the foresters who shared the drenching rains and muddy trails with the botanists on the field surveys.

Actually, the first survey party in Colombia whose work is discussed by Dr. Steere was supervised by a forester and included two other foresters in addition to the two botanists and one chemist. If credit were to be given or even implied local B.E.W. (F.E.A.) officials as well as many individuals of the countries surveyed should be included also for their part in the work.

None would deny that Dr. Steere and the other botanists played an extremely important role in the cinchona surveys, and it is understood that any elimination was not done purposely, but rather, unintentionally in developing the interesting botanical notes. However, this supplementary mention of the part played by the forestry profession in the surveys seemed desirable, not to change the botanical discussions, but to clarify to any one not acquainted with the makeup of the missions the greater breadth of the crews who located and moved the cinchona plants.

L. R. HOLDRIDGE

FORESTRY DIVISION,
SOCIÉTÉ HAÏTIANO-AMÉRICAIN
DE DÉVELOPPEMENT AGRICOLE.
PORT AU PRINCE, HAÏTI

STARS IN AMERICAN MEN OF SCIENCE

I HAVE read with interest and some amusement the comments of S. S. Visser in the March 16, 1945, issue of SCIENCE on "Comparative University Strength in Scientists Starred in 'American Men of Science'—VII."

It is my opinion that there is no true philosophical or scientific basis for the system of starring and, therefore, all investigations pyramided on the assumptions of starring are negative and, perhaps, even vicious. They have led, however, to many amusing conclusions, not the least of which is Visser's.

It might be more instructive to analyze the universities which Visser has selected, not only from the point of view of the relation of starred faculty members to the total faculty members, but what constitutes the universities under consideration and also their comparative endowments. For example, we see on Visser's list that Pennsylvania has fourteen starred members out of the teaching staff of 1,322, while Princeton has twenty-six starred members out of a teaching staff of 220 and Harvard has fifty starred members out of a total of 1,775.

Harvard and Pennsylvania have medical and dental schools, which Princeton has not. Harvard and

Pennsylvania have law schools and certain other graduate bodies which, so far as I am aware, do not adorn old Nassau. Therefore, I think that Visser's inquiries should be confined to the fields in which men are starred. For according to Visser's analyses the Divinity School of Harvard is a liability rather than an asset when it comes to the proportion of men starred.

Princeton has a larger endowment than Pennsylvania, although apparently it has about one sixth of the faculty of Pennsylvania. Harvard has over four or five times the endowment of Pennsylvania and about 25 per cent. more faculty members. Harvard is usually considered the wealthiest university and yet, I believe, its annual income is no greater than certain state universities, whose appropriations by State Legislatures run into the millions. Neither Harvard nor Princeton receive money, as far as I am aware, from their respective states, and although Pennsylvania is not a state university, it does receive some state aid.

I recommend, therefore, that the next analysis of starred men takes into consideration the comparative wealth of the institution, not only from the point of view of endowment but also from the point of view of annual income from state, students and endowment.

A comparative salary study of professorships and other ranks in relation to starring should afford interesting instruction. I should like to mention that there are certain personality traits in institutions which should be likewise considered. Institutions, like persons, belong to upper, middle and lower classes, and by this is meant psycho-biological classification, not a social one. It is made of such factors as age, wealth, tradition, attitudes, vitality, connections, graduates and the like which constantly change and thus change the classification. It is this psycho-biological classification to which we refer when we say that such and such a place is not what it used to be; we refer to it in such terms as "The Big Three"; fresh-water colleges; or diploma mills, etc. I should also like to observe that some universities like Johns Hopkins or the Massachusetts Institute of Technology are more "national" in personality in contrast to certain other universities which seem to be of a more "local" nature. Such personality traits work an influence in attracting men and minds, in forming opinions; and perhaps even on taxonomists of universities and their faculties.

RICHARD W. FOSTER

EMPLOYMENT AFTER THE WAR

IN Dr. Joseph Mayer's article published in SCIENCE for April 13, it seems to me that two important agencies have been overlooked: (1) An organization to study the needs in goods, qualitatively and quanti-

tatively, of the country and (with a view to exports) of the world. For example, what is needed to keep all the people as physically fit as their natures will permit? (2) A great development of adult education,

fitting the people to do the needed work. The astonishing success of the war workers shows how adaptable people are, if really interested and efficiently taught.

T. D. A. COCKERELL

SPECIAL ARTICLES

PRODUCTION OF IMMUNITY TO DENGUE WITH VIRUS MODIFIED BY PROPAGATION IN MICE¹

THE purpose of this preliminary communication is to report, (a) the successful propagation of dengue virus in mice, and, (b) that beginning with the 7th passage in mice the virus had undergone such extensive modification in its pathogenic properties for human beings that consideration of its use as a vaccine seemed justifiable.

The work to be reported here is part of a systematic investigation of the virus of dengue with special emphasis on those of its properties which might lend themselves to the development of a vaccine. The work was carried on with five strains of dengue virus isolated by one of us (A.B.S.) from outbreaks of the disease in Hawaii and New Guinea.² The identity of the virus was established (a) by its capacity to produce in human volunteers a disease characterized by a fever of 4 to 7 days' duration, severe pain in various parts of the body, rash, lymphadenopathy and leukopenia with certain changes in the leukocytic formula, and (b) by its transmission after a suitable extrinsic incubation period by relatively small numbers of *Aedes aegypti* mosquitoes.³ Most of the studies were carried out with the Hawaiian strain of the virus for the following reasons: (a) it was the most virulent in the sense that it produced the most severe disease in human volunteers; (b) about 1,000,000 minimal human infective doses per cc were

found in the serum of experimental cases during the first 24 hours of the disease,⁴ and (c) having found that it had a particle size in the range of 20 mμ it was possible to obtain concentrates of the virus possessing more than 10,000,000 minimal human infective doses per cc by centrifugation at 24,000 r.p.m. for 15 minutes in an 8-inch rotor.^{4,5} With these concentrated preparations of virus an exhaustive effort was made to obtain growth in cultures containing monkey embryo tissues and in embryonated chicken eggs of various ages, inoculated by various routes and incubated for varying periods at different temperatures but with negative results. After 2 or more passages the cultures produced neither disease nor immunity upon inoculation in human beings.

Dinger and Snijders⁶ in 1931 attempted to propagate dengue virus from the Dutch East Indies by intracerebral inoculation of mice, but without success. Our own initial attempts to infect young mice in the same manner with human serum of proved infectivity were also regarded as negative, but it must be stated that the mice were observed only for gross signs of involvement of the nervous system for the usual period of 2 to 3 weeks. In the first two attempts with concentrated, ultracentrifuged Hawaii virus, there was an occasional mouse that died or exhibited signs of nervous system involvement, but after one or two further passages negative results were obtained. On the third attempt with intracerebral inoculation of concentrated, ultracentrifuged Hawaii virus in 10 to 12-day old Swiss albino mice, it proved possible to transmit in series an agent which produced vaguely discernible to severe signs of nervous system involvement in a varying, and initially very small, proportion of the inoculated mice. However, 16 serial passages have now been completed and the tests with mouse-passaged material in human volunteers have established that the virus propagated in mice is dengue. Only 10 to 20 per cent. of the inoculated mice at first exhibited clinical signs of the infection (sometimes limited to slight weakness of the extremities demonstrable only by special tests), and the incubation period was frequently 3 to 4 weeks. Beginning with the 6th passage the incubation period

¹ This investigation was sponsored by the Commission on Neurotropic Virus Diseases, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of The Surgeon General, U. S. Army, Washington, D. C. The laboratory work was carried out at The Rockefeller Institute for Medical Research, Princeton, N. J., and we wish to express our indebtedness to Dr. H. S. Gasser and Dr. C. TenBroeck for the facilities which were provided us. The participation of the inmates of the New Jersey State Prison at Trenton, N. J., who volunteered, without any offer of reward, to serve as subjects in these experiments, and the cooperation of the late Commissioner William J. Ellis, of the Department of Institutions and Agencies of the State of New Jersey, in providing facilities for this work at the N. J. State Prison, are hereby gratefully acknowledged.

² The specimens from Hawaii were provided on March 6, 1944, by Lt. Col. Clarence S. Moran, M.C., commanding the Central Pacific Area Laboratory, and those from New Guinea by Lt. Col. Cornelius B. Philip, Sn.C., of the U.S.A. Typhus Commission.

³ Our associate, Capt. Wm. G. Jahnes, Jr., Sn.C., raised and took care of the mosquitoes used in these investigations.

⁴ A. B. Sabin. Unpublished observations on dengue.

⁵ We are indebted to Dr. Wendell M. Stanley for his help in the ultracentrifugation work.

⁶ J. E. Dinger and E. P. Snijders, *Arch. f. Schiff's Tropenhyg.*, 35: 498, 1931.

has been more often in the range of 2 weeks, and the incidence of manifest paralysis with fatal termination has increased especially since the 9th passage. However, only about 60 to 75 per cent. of the inoculated mice exhibited clinical signs of the infection as late as the 13th passage. In the 14th passage, 90 per cent. of 20 approximately 3-weeks-old mice developed distinct central nervous system (C.N.S.) signs, but only 1 of 10 six-weeks-old mice exhibited the same signs, indicating the importance of using young mice for routine passage. In the 15th passage all 10 approximately 3-weeks-old Swiss mice developed C.N.S. signs, but of 10 mice of about the same age of an albino strain bred for many years at the Rockefeller Institute at Princeton, N. J., only 1 was affected. Simultaneous tests with 5th passage virus on other breeds of mice (6 varieties obtained from the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine, and a group of brother-sister inbred Swiss albino mice for which we are indebted to Dr. Clara Lynch, of the Rockefeller Institute in New York) have indicated that different "strains" of mice may vary in their capacity to develop clinical signs of infection. The "dba" (dilute brown non-agouti) strain obtained from Bar Harbor appeared to be the most susceptible.

The mouse-passaged dengue virus was not pathogenic for cotton rats and guinea pigs (passage V and XIII) or for hamsters and rabbits (passage V). This limited host range may be used to differentiate it from two groups of viruses occasionally carried spontaneously by mice, *i.e.*, lymphocytic choriomeningitis and the encephalomyelitis viruses isolated by Theiler. A preliminary pathological study of the central nervous system of mice infected with dengue virus indicates that the attack is not on the meninges or the ependymal structures; it would appear that the neurones are affected, but the actual number of neuronal and infiltrative lesions is relatively small even in mice that are completely paralyzed or die of the infection.

The following attempts have been made to determine whether or not serial propagation of dengue virus in mice may be initiated *without* using concentrated, ultracentrifuged virus. In addition to inoculating undiluted, infectious human sera we also injected the 1:10, 1:100, and 1:1000 dilutions in 10 per cent. normal human serum-Tyrode's solution, and the best results were obtained with the 1:100 dilution.⁷ The data seemed to suggest that the sera may perhaps contain an "inhibitor" as well as virus, and that either concentration of the virus by centrifuga-

tion or dilution of the "inhibitor" may achieve a suitable ratio between the two. Although three consecutive passages have been accomplished thus far in a series initiated with one diluted serum, the same difficulties were encountered in adaptation of the virus to mice, *i.e.*, initial low incidence of clinical signs, long incubation periods, necessity of using large numbers of young mice and persistence in repeating negative passages. When a suspension of dengue-infected *Aedes aegypti* mosquitoes was injected intracerebrally in mice, only 2 out of 20 exhibited clinical signs of infection, and a second passage did not yield any better results.

Thus far, in addition to the Hawaii strain of dengue virus, it has been possible to obtain positive serial passage in mice also with the New Guinea "A" strain which is immunologically identical with it.⁴ The New Guinea "B," "C" and "D" strains, which, while related to the Hawaii strain, are, nevertheless, immunologically distinct,⁴ thus far have yielded negative results, but further attempts to adapt them to mice are still in progress.

The decision to test the mouse-passaged virus in human beings was not made until 5 passages in mice (requiring about 3 months) had indicated that we were dealing with an agent unlike any other hitherto described. Sixteen human volunteers have now been inoculated with various passages of the mouse-adapted virus—pool of 2nd and 3rd (1), 4th and 5th (1), 5th (3), 6th (2), 7th (3), 9th (2), 10th (4). Like the original virus in human serum,⁴ the mouse-adapted virus produced skin lesions at the sites of intracutaneous injection, and 6 to 9 days after inoculation systemic manifestations, including fever, very marked maculo-papular and petechial rash, leukopenia and enlargement of certain lymph nodes. Immunity to infection with the regular dengue virus invariably followed. Although it was evident from the beginning that the virus had undergone a change even as a result of 2 serial passages in mice, fairly severe types of experimental dengue infection were produced in some of the volunteers inoculated with virus from the first 6 passages. 0.2 cc of a 1:1000 dilution of centrifuged brain and cord suspension from a pool of 5th-passage mice was sufficient to produce the disease in man and there were indications from skin reactions that a smaller dose might also have been infective. The virus was demonstrated in the blood of the inoculated human volunteers and transmission by *Aedes aegypti* was accomplished, although relatively large numbers of mosquitoes and an extrinsic incubation period of 3 weeks or longer (10 to 14 days is usual for the unmodified virus) seems to have been required.

Tests with the 7th, 9th and 10th passage material

⁷ The diluted sera were inoculated at the suggestion of Dr. Max Theiler, of the International Health Division of The Rockefeller Foundation, in view of his observations on the primary transmission of certain strains of yellow fever virus to mice.

on 9 volunteers indicated that the mouse-adapted dengue virus had undergone a very extensive modification in its pathogenicity for human beings. The intracutaneous or subcutaneous injection of 0.2 cc of a 5 per cent. centrifuged brain and cord suspension gave rise either to no systemic symptoms or after an incubation period of 8 to 10 days to reactions not exceeding in severity those following typhoid vaccination, i.e., fever with or without headache and malaise for 24 hours or less. A marked and extensive maculo-papular eruption and terminally also petechiae on the feet and ankles were the rule. However, when this dose of mouse-adapted dengue virus was given simultaneously, or mixed, with the regular U. S. Army dose of yellow fever vaccine, the rash was reduced to a small number of faint macules and the petechiae were entirely suppressed. This combination was tried because one of us (A.B.S.) had previously observed an interference phenomenon between yellow fever vaccine and the regular, unmodified dengue virus in human beings.⁴ It has, furthermore, been demonstrated that the virus present in the blood at the onset of the rash in the volunteers inoculated with 7th passage virus was of the modified type, and that *Aedes aegypti* feeding during that period became infected with difficulty since large numbers of mosquitoes and an extrinsic incubation of more than 3 weeks were required to transmit the virus. However, the virus that these mosquitoes transmitted was also of the modified type, since rash without fever or significant symptoms and the leukocyte changes seen in dengue were the only reactions observed in the bitten individual. The 9 volunteers who were inoculated with the 7th, 9th or 10th mouse-passage dengue virus, either alone or in combination with yellow fever vaccine, and 1 volunteer who was bitten by mosquitoes carrying the modified virus, were all found to be immune when they were exposed to the bites of *Aedes aegypti* mosquitoes of proved infectivity at intervals of 12 days (2 men), 21 days (5 men), 24 days (1 man) and 28 days (2 men) after inoculation. Four volunteers, who served as controls for these tests and were bitten by mosquitoes from the same lots, developed typically severe unmodified dengue. The volunteers, who received the combination of dengue and yellow fever vaccine, also developed neutralizing antibodies for the yellow fever virus.⁸

SUMMARY

It has been demonstrated that dengue virus can be propagated by intracerebral inoculation in mice. Although initial adaptation to the mouse is a tedious

and difficult process, 16 consecutive passages have been achieved already in one series and further passages are in progress. The virus propagated in mice produced dengue in human volunteers, but was not pathogenic for cotton rats, hamsters, guinea pigs or rabbits. Although it was evident that even after 2 serial passages in mice the virus produced a modified type of disease in human beings, tests with the 7th, 9th and 10th passage material indicated that the modification had become so marked that it could be used as a vaccine for the production of immunity against dengue.

LT. COL. ALBERT B. SABIN, M.C., AUS

CAPT. R. WALTER SCHLESINGER, M.C., AUS
ARMY EPIDEMIOLOGICAL BOARD,
THE CHILDREN'S HOSPITAL
RESEARCH FOUNDATION,
CINCINNATI 29, OHIO

BACTERIOSTATIC AND BACTERICIDAL PROPERTIES OF 2,4-DICHLOROPHENOXYACETIC ACID

THE specificity of 2,4-dichlorophenoxyacetic acid in bringing about the death of certain weeds^{1, 2} and the well-known bacteriostatic properties of some other aromatic compounds suggest that 2,4-dichlorophenoxyacetic acid might affect the growth of some lower organisms such as fungi and bacteria.

It was observed that open test-tubes of potato-dextrose agar³ containing 0.1 per cent. 2,4-dichlorophenoxyacetic acid dissolved in 0.5 per cent. Carbowax 1500⁴ remained sterile for 30 days, while similar tubes containing no 2,4-dichlorophenoxyacetic acid became contaminated with bacteria and fungi.

In a subsequent experiment two lots of potato-dextrose agar were prepared, one containing 0.1 per cent. of 2,4-dichlorophenoxyacetic acid and 0.5 per cent. Carbowax 1500 and the other containing 0.5 per cent. Carbowax only. The reaction was adjusted with N/1 NaOH to give pH values of 5, 6, 7 and 8, respectively, in aliquots of each of the two series. All manipulations involving the media were made in the open laboratory. The media and utensils used were not sterilized and no attempt was made to avoid contamination. Five Petri dishes were used for each medium, 15 ml being used for each dish. After the media had solidified, spores of *Penicillium* sp. were dusted over the surface of all plates. The plates were then closed and incubated at 28° C. Within two days colonies of

¹ J. W. Mitchell, F. F. Davis and P. C. Marth, *Golfdom*, October, 1944.

² P. C. Marth and J. W. Mitchell, "2,4-Dichlorophenoxyacetic Acid as a Differential Herbicide," *Botanical Gazette*, 106: 224-232, 1944.

³ 200 gms peeled potatoes, 20 gms dextrose, 15 gms agar, 1,000 ml water.

⁴ J. W. Mitchell and C. L. Hamner, *Bot. Gaz.*, 105: 474-483, 1944.

⁸ We are indebted to Dr. Max Theiler, of the International Health Division of The Rockefeller Foundation, for carrying out the yellow fever neutralization tests on these sera.

*Bacillus subtilis*⁵ and the *Penicillium* sp. were observed on all the control plates from pH 5 through pH 8. No colonies of bacteria were observed on the 2,4-dichlorophenoxyacetic acid media at pH 5, 6 or 7, but some very small apparently static colonies about 3 mm in diameter appeared on the treated agar at pH 8. These colonies were not visible a few days after their appearance. The bacteria overran the control plates at pH 7 and 8 so rapidly that the fungus barely made pin-point spots before the surfaces of the media were covered with bacteria, thus checking the growth of the fungus. The *Penicillium* sp. grew vigorously on all media treated with 2,4-dichlorophenoxyacetic acid except that at pH 8 in which case its growth was somewhat limited probably because of the relatively high alkalinity. There was no apparent antagonism between the fungus and the bacteria. The relative appearance of these plates remained unchanged for 15 days, even though they were opened on several occasions after 3 days' incubation.

For a further test of this bacteriostatic action of the Carbowax-acid mixture, two lots of potato-dextrose agar were prepared; one contained 0.1 per cent. of the acid and 0.5 per cent. of Carbowax; the other 0.5 per cent. of Carbowax. The acid-treated medium was diluted with the Carbowax medium to give concentrations of 0.02, 0.04, 0.06 and 0.08 per cent. of the acid, one lot was maintained at 0.1 per cent. and one lot was of Carbowax control agar. N/1 NaOH was added so that media at each concentration of 2,4-dichlorophenoxyacetic acid were represented at pH 6 and pH 7. The Carbowax control was also adjusted to pH 6 and pH 7. These media were then autoclaved 15 minutes at 15 pounds steam pressure and 15 ml poured in each Petri dish. After cooling, 5 plates of each medium were then inoculated on the left side with mycelial transfers of a *Fusarium* sp., streaked on the right side with *Aerobacter cloacae* isolated from bean plants, and streaked down the center of the plate with *Bacillus subtilis*, which had appeared in the control plates of the previous test. The plates were incubated at 28° C. After two days' incubation the fungus was growing vigorously in all plates. However, there was a definite bacteriostatic effect on both bacteria at all concentrations. The growth of *B. subtilis* was retarded more than that of *A. cloacae* and at 0.08 per cent. concentration the former was completely inhibited, while the latter appeared to be definitely retarded. Very slight growth of both bacteria took place at the 0.1 per cent. concentration of 2,4-dichlorophenoxyacetic acid. After one week the inhibiting effect was more pronounced

and transfers were made to potato-dextrose agar from the margins and from the centers of the streaks of *A. cloacae* which had grown in the medium containing 0.5 per cent. Carbowax and 0.08 per cent. of the acid. There was no growth from the marginal transfers, or from 4 out of 5 of the central transfers, and it was concluded that most of the bacteria had been unable to maintain growth in the 0.08 per cent. concentration. The *Fusarium* sp. grew well at all concentrations.

In order to determine what role the Carbowax might play in the action of the acid, the sodium salt, which is soluble in water, was prepared by adding N/1 NaOH to 2,4-dichlorophenoxyacetic acid. The media used were: (1) potato-dextrose agar + 0.02 per cent. of the Na salt + 0.5 per cent. Carbowax; (2) potato-dextrose agar + 0.08 per cent. of the Na salt + 0.5 per cent. Carbowax; (3) potato-dextrose agar + 0.02 per cent. of the Na salt, and (4) potato-dextrose agar + 0.08 per cent. of the Na salt. Control media consisted of one lot of plain potato-dextrose agar and one lot of potato-dextrose agar containing 0.5 per cent. Carbowax. These media were adjusted to pH 7 with N/1 NaOH, sterilized at 15 pounds steam pressure for 20 minutes and 15 ml poured into 9 cm Petri dishes. After cooling, ten plates of each medium were streaked with three bacteria, *Bacillus subtilis*, *Staphylococcus aureus* (Food and Drug Administration strain 209) and *Phytomonas tumefaciens* (strain 671 Plant Industry Station, Beltsville, Md.)

At 0.02 per cent. concentration of the sodium salt of 2,4-dichlorophenoxyacetic acid there was a decided retarding effect on the growth of all three bacteria. Eight hundredths per cent. concentration of the salt completely inhibited *S. aureus* and *P. tumefaciens*, and with *B. subtilis* there was just a faint cloudiness visible along the streak.

The presence or absence of the Carbowax 1500 had little effect on the action of the sodium salt of 2,4-dichlorophenoxyacetic acid, although there were some indications that the salt alone at 0.02 per cent. had a greater retarding effect than the salt in combination with Carbowax 1500.

In a subsequent test it was found that 0.08 per cent. of the sodium salt of 2,4-dichlorophenoxyacetic acid in potato-dextrose agar completely inhibited *B. subtilis* but had no apparent effect on the growth of *Penicillium notatum* (strain 1249-B21 Northern Regional Research Laboratory) when the two were grown in the same Petri dish.

The salient points observed in these limited tests are that the addition of 0.02 per cent. 2,4-dichlorophenoxyacetic acid or its sodium salt with or without 0.5 per cent. Carbowax into potato-dextrose agar had a decided retarding effect on the growth of *Bacillus*

⁵ Identified by N. R. Smith, Bureau of Plant Industry, Soils, and Agricultural Engineering, Agriculture Research Administration, U. S. Department of Agriculture, Beltsville, Md.

subtilis, *Aerobacter cloacae*, *Staphylococcus aureus* and *Phytomonas tumefaciens*, while it had no apparent effect on the growth of *Fusarium* sp. and *Penicillium* sp. A concentration of 0.08 per cent. of 2,4-dichlorophenoxyacetic acid or its sodium salt in potato-dextrose agar with or without 0.5 per cent. Carbowax prevented the growth of *B. subtilis*, *S. aureus* and *P. tumefaciens* and retarded the growth of *A. cloacae*, being toxic to this organism in 4 out of 5 cases after a period of one week. The growth of *Fusarium* sp. and *Penicillium* sp. was not affected noticeably by the 0.08 per cent. concentration of the acid or its salt nor was the growth of *P. notatum* visibly affected by the salt.

Further studies are in progress using common test organisms and a number of plant pathogens.

E. C. STEVENSON,
Associate Pathologist
JOHN W. MITCHELL,
Physiologist

BUREAU OF PLANT INDUSTRY, SOILS AND
AGRICULTURAL ENGINEERING,
U. S. DEPARTMENT OF AGRICULTURE,
BELTSVILLE, MD.

THE PRODUCTION OF CARCINOMA AND SARCOMA IN TRANSPLANTED EMBRYONIC TISSUES¹

SEVERAL years ago it was found that embryonic mammalian tissues could be grown in adult alien species and that such transfer was as readily effected as homologous embryonic transplantation.² At the same time an attempt was made to induce tumor formation in heterologous embryonic transplants with chemical carcinogens; for control parallel experiments with homologous embryonic tissues were performed. Cancer resulted in a number of heterologous transplants, including several of human origin; but an exploration of the diverse lines of research suggested by the results is still in progress and demands a more detailed report than is possible at present. The results of the control studies entailing the production of cancer in homologous embryonic transplants appear of sufficient immediate interest to warrant an independent report at this time. The intent of the present note is to draw attention to the method and its general results. Precise details and other pertinent observations will be discussed in a later paper.

The technique employed is comparable to that used in routine tumor or tissue transfer. The embryonic organ or tissue is placed in the mouth of a trocar and

impregnated with crystals of methyleholanthrene. The trocar is inserted through an incision and the tissue fragment expelled in the desired region of the new host. The anterior chamber of the eye, testicle, peritoneal cavity, muscle and subcutaneous regions have been utilized as inoculation sites but, in general, subcutaneous transfers have proved most satisfactory. Mouse embryos have been used most extensively in homologous transfers, but in several experiments guinea-pig embryos were utilized, and it is significant that despite the resistance of adult animals of this species, the embryonic tissues proved as susceptible to the carcinogenic action of methyleholanthrene as did mouse material.

In experiments utilizing mice, treated embryonic tissue was transferred to adult animals of the same and of different strains without apparent variation in the incidence of takes or in the ultimate fate of the transplant. The organs from embryos of C₃H extraction grew as readily in C57 black or Bagg albino mice as in the parent strain, and present data reflect no influence of the genetic constitution of the new host on the action of the carcinogenic chemical.

A variety of embryonic organs and tissues, including lung, stomach, intestine, skin, muscle and cartilage, have been employed with comparable results. Successful transfer is followed by rapid growth which reaches a peak toward the end of the second week. A short interval of apparent quiescence ensues, but early in the fourth week renewed growth becomes evident. The transplants in animals killed between the thirtieth and thirty-fifth days measure 1 to 1.5 cm in diameter and show all the cellular and structural changes characteristic of cancer. It should be emphasized that in all these experiments, the diagnosis of cancer is based on biological behavior as well as on morphology and such diagnosis is not made unless the tissue in question possesses the ability to grow and to duplicate its structure in alien species. At the present point in this series of experiments, approximately 60 per cent. of the transplants examined between the thirtieth and thirty-fifth days fulfil both morphological and biological requirements. It appears significant that embryonic tissues undergo such modifications within 35 days, whereas from 90 to 200 or more days are required before comparable changes appear in adult tissues.

In view of present efforts directed toward the production of cancer of the alimentary canal with chemical carcinogens, it is noteworthy that carcinoma of the glandular portion of the stomach and of the intestine may be induced by the application of the chemicals to embryonic transplants. A pronounced hyperplasia precedes the appearance of malignant changes and, in the intestine, results in glandular

¹ From the Departments of Pathology and Surgery, Yale University School of Medicine, New Haven, Conn. This investigation was supported by grants from the Jane Coffin Childs Memorial Fund for Medical Research and the International Cancer Research Foundation.

² H. S. N. Greene, *Cancer Research*, 3: 809, 1943.

masses simulating polyps. Gastric mucosa produces an abundance of mucin in early stages and may terminate either as a colloid carcinoma or a typical fundic adenocarcinoma.

Involvement of host tissues is apparent by the forty-fifth day and is characterized by the active invasion of tissues as well as by the passive infiltration of tissue spaces. Metastasis has occurred, but the majority of animals have been killed for early study and significant data are not yet available.

The carcinomas arising in subcutaneous regions are obviously derived from the transplanted embryonic organ, but some question obtains with reference to the origin of the sarcomas, for their appearance is often identical with that of growths obtained in adult animals. However, their early inception together with their position in relation to embryonic remnants is suggestive. Moreover, in one instance in which the primary tumor consisted solely of sarcomatous fibroblasts, a splenic metastasis contained areas of newly formed cartilage, thus identifying the growth as a chondrosarcoma and rendering an origin from the subcutaneous connective tissue of the adult host highly improbable.

These experiments were instituted on the assumption that the reserve stores of stem or partially differentiated cells of the body formed the source of neoplastic cells in adult animals and that embryonic tissues might prove a more favorable medium for the experimental production of tumors than the corresponding tissues of adult animals. The results obtained support this assumption. The method described offers a means of producing carcinomas in a

variety of internal organs in a relatively short time. Moreover, the ability to transplant treated tissues heterologously and to test the susceptibility of embryonic organs of resistant species after transfer to susceptible hosts and vice versa offers a new approach to a study of the nature and mode of action of carcinogenic chemicals.

HARRY S. N. GREENE

ACETYL CHOLINE AND THE ACTIVATION OF MARINE EGGS

RECENT studies have made it appear probable that acetyl choline is of fundamental importance in the excitation process in nerves, muscles and electric organs.^{1, 2} The activation of marine eggs has certain features in common with excitation of nerve,³ and it seemed worth while to examine the effects of acetyl choline on such activation.

The eggs of the echiuroid worm *Urechis caupo* Fisher and MacGinitie, and of the sea urchin *Strongylocentrotus purpuratus* (Stimpson) were used. *Strongylocentrotus* eggs were activated by (a) very dilute sperm suspensions or (b) treatment with distilled water for $\frac{1}{2}$ to 2 minutes. *Urechis* eggs were activated by (a) dilute sperm suspensions, (b) brief treatment with hypotonic sea water or distilled water, (c) treatment with isotonic calcium chloride solution

¹ J. F. Fulton and D. Nachmansohn, *SCIENCE*, 97: 569, 1943.

² D. Nachmansohn, R. T. Cox, C. W. Coates and A. L. Machado, *Jour. Neurophysiol.*, 5: 499, 1942, and 6: 383, 1943.

³ R. S. Lillie, "Protoplasmic Action and Nervous Action," Chicago, 1932 (2nd ed.).

TABLE 1
INHIBITION OF ACTIVATION IN MARINE EGGS BY ACETYL CHOLINE AND PHYSOSTIGMINE

Eggs of:	Activating agent:	Per cent. of eggs activated, controls	Difference from control, and standard error of the difference, with	
			acetyl choline	physostigmine
<i>Urechis caupo</i>	Dilute sperm	93	-93 ± 2	
		64	-64 ± 2	
		87		-67 ± 3
		72		-16 ± 3.5
		58		-27 ± 7
	Hypotonic sea water	24		+63 ± 8
		35	-29 ± 3	-26 ± 3
		97	-15 ± 2.4	-7 ± 1.7
		22	-20 ± 3	-22 ± 3
		17	-15 ± 3	-16 ± 3
	Ca-free artificial sea water	87	-87 ± 2	
		9	-8 ± 1	
		4	-4 ± 1	
	Ultraviolet	97		-96 ± 1
		68		-41 ± 7
		93	-92 ± 2	-80 ± 3
<i>Strongylocentrotus purpuratus</i>	Dilute sperm	42	-41 ± 4	-40 ± 5
		22	-21 ± 3	-21 ± 3
		64	-60 ± 3	+12 ± 3.5
		19		+16 ± 5
	Distilled water	5.8	-5.6 ± 1.1	+0.9 ± 1.6
		40	-39 ± 2	-27 ± 3
		37	-37 ± 2	-25 ± 3
		30	-29 ± 2	-11 ± 3

for 10-20 minutes, (d) treatment with artificial sea water lacking calcium ion for 1 to 4 hours, or (e) irradiation with ultra-violet light of wave-length about 2537 Å for $\frac{1}{2}$ to 3 minutes. Membrane elevation was used as a criterion of activation in *Strongylocentrotus* eggs, dissolution of the germinal vesicle in the eggs of *Urechis*. A small and variable percentage of the eggs of *Urechis* cleaved when activated by any of the artificial treatments. Artificial activation of *Strongylocentrotus* eggs did not result in cleavage.

The addition of 1 mg of acetyl choline bromide to 10 ml of the activating solution before the eggs were placed in the solution resulted, in almost every case, in a marked decrease in the number of eggs activated by the particular treatment. Typical results are presented in Table 1. The addition of 1 mg of physostigmine salicylate to 10 ml of activating solution had effects wholly comparable to those of acetyl choline, except when the eggs were activated with sperm. With the eggs of *Strongylocentrotus* activated by sperm, the only effect noted was a small increase in activation. With the eggs of *Urechis* activated by sperm, a marked decrease similar to that produced by acetyl choline was evident in most cases, but in one experiment an equally marked increase was apparent.

Further analysis of these effects is in progress, and a more detailed account will be published later.

BRADLEY T. SCHEER

WM. G. KERCKHOFF MARINE LABORATORY,
CALIFORNIA INSTITUTE OF TECHNOLOGY

THE OXYDASE REACTION IN CHICK EMBRYOS AND BROTH MEDIA CONTAINING NEISSERIA^{1, 2}

THE value of the oxydase reaction described by Gordon and McLeod³ for the preliminary identification of meningococci and gonococci has been well established. This reaction is ordinarily elicited by spraying or flooding a petri dish culture with a fresh, one per cent. aqueous solution of either dimethyl or tetramethyl paraphenylene diamine hydrochloride. Colonies of members of the genus *Neisseria* will then undergo a series of characteristic color changes: pink to maroon to black with the former reagent, and lavender to purple with the latter.

In the course of certain experiments concerned with meningococci and gonococci^{4, 5} infections of chick

embryos, it was found that typical oxydase reactions could be produced upon the infected chorio-allantoic membranes. Forty-eight hours after the inoculation⁶ of the chorio-allantoic membranes of eleven-day-old embryos a portion of the shell was removed, the membrane cultured, and a drop of either the dimethyl or tetramethyl paraphenylene diamine hydrochloride solutions deposited thereon. In all instances the *Neisseria*-infected chorio-allantoic membranes gave positive reactions. Control embryos, either uninfected or infected with organisms other than the *Neisseria*, yielded negative reactions. Parallel passages on appropriate solid media gave similar findings.

Since the allantoic fluids of *Neisseria*-infected embryos contain large numbers of organisms, they were subjected to similar tests. This was achieved by overlaying one milliliter of allantoic fluid in a narrow tube with one or two drops of oxydase reagent. The typical sequences of color changes were noted at the interphase. Similar reactions were obtained in broth cultures, including those in the *Neisseria* fermentation broth previously described.⁷

The specificity of the reaction in both infected allantoic fluid and broth media suggested the possibility that the reacting enzyme was of a soluble character.

TABLE 1

SUMMARY OF OXYDASE REACTIONS OBTAINED IN CHICK EMBRYOS INFECTED WITH VARIOUS AGENTS

Infecting agent	Total number strains	Total number embryos	Chorio-allantoic membrane		Allantoic fluid*		Supernate†	
			Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
<i>N. intracellularis</i>	15	41	18	0	23	0	22‡	1
<i>N. gonorrhoeae</i>	3	13	12	0	1	0	N.D.§	N.D.
<i>N. catarrhalis</i>	1	2	2	0	N.D.	N.D.	N.D.	N.D.
<i>Staph. aureus</i>	2	2	0	2	N.D.	N.D.	N.D.	N.D.
<i>Sh. alkalescens</i>	1	2	0	2	N.D.	N.D.	N.D.	N.D.
<i>Sh. paradys.</i>	1	2	0	2	N.D.	N.D.	N.D.	N.D.
Boyd 88	2	4	0	2	0	2	0	2
Paracolon	1	1	0	1	0	1	N.D.	N.D.
<i>P. gallinaceum</i>	1	1	0	1	0	1	N.D.	N.D.
Influenza A virus	1	2	0	2	0	2	0	2
Normal embryos	..	8	0	8	0	1	0	1

* Uncentrifuged.

† Centrifuged, bacteria-free.

‡ The allantoic fluid whose cell-free supernate gave a negative reaction was also negative on culture but morphologically and tinctorially positive for *N. intracellularis* on smear examination.

§ N.D. = Not done.

⁶ The surface of a chocolate agar culture which had been incubated for twenty-four hours was scraped and the growth suspended in tryptose-phosphate broth. One drop of this heavy suspension served as the inoculation dose.

⁷ D. M. Kuhns and H. A. Feldman, *Am. Jour. Pub. Health*, 33: 1461-65, 1943.

¹ With the technical assistance of Frances S. Friedman.

² The valuable aid of First Lieutenant (then Sgt.) Barclay R. McGhee, Sn. C., A. U. S., during the early phases of this study is gratefully acknowledged.

³ J. Gordon and J. W. McLeod, *Jour. Path. and Bact.*, 31: 185-190, 1928.

⁴ G. J. Buddingh and A. D. Polk, *Science*, 86: 20-21, 1937.

⁵ G. Morrow and G. P. Berry, *Jour. Bact.*, 36: 280, 1938.

acter. To determine this a number of infected allantoic fluids were centrifuged until the supernates no longer gave positive cultures. With one exception bacteria-free allantoic fluids yielded reactions similar to those obtained prior to centrifugation.

The data are summarized in Table 1.

CONCLUSIONS

(1) Specific oxydase reactions may be obtained with solutions of either dimethyl or tetramethyl para-

phenylene diamine hydrochloride when the following are infected with *Neisseria*: the surface of the chorio-allantoic membranes of chick embryos, allantoic fluids both before and after the removal of the infecting bacteria and suitable broth media.

(2) The enzyme responsible for the positive oxydase reaction elicited with the *Neisseria* is soluble and diffuses into the surrounding liquid environment.

HARRY A. FELDMAN,

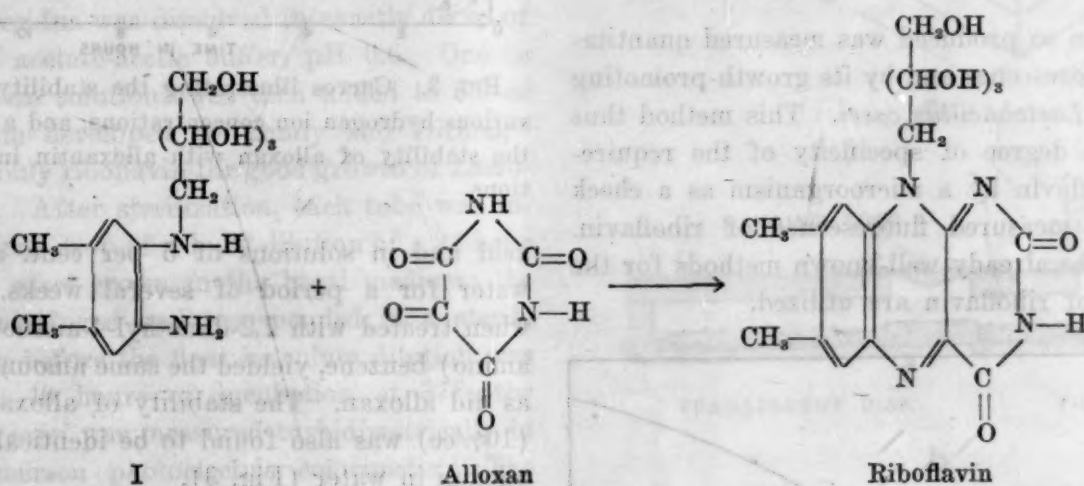
Major, Medical Corps, A.U.S.

SCIENTIFIC APPARATUS AND LABORATORY METHODS

A MICROBIOLOGICAL AND FLUOROMETRIC TEST FOR MINUTE AMOUNTS OF ALLOXAN^{1,2}

The work of Dunn and coworkers^{3,4} has revealed that alloxan administered parenterally produces in rats and rabbits an acute specific necrosis of the islets of Langerhans. This has been amply confirmed in rats, rabbits, dogs and monkeys by various workers.⁵⁻¹⁰ The production of experimental diabetes by

play some role in the etiology of diabetes mellitus. For the study of the metabolism of alloxan, a specific method for the determination of alloxan would obviously be advantageous. In the present note, we wish to report our preliminary studies leading to a sensitive and specific test for the quantitative estimation of alloxan in pure solution, which we hope may eventually lead to a specific method applicable to biological materials.



alloxan and the importance of these experiments has been reviewed by Joslin.^{11,12} It has been suggested by Dunn and his coworkers⁴ that possible defects in the metabolism of purines or of alloxan in man may

At the time this work was undertaken, no specific method for alloxan was available. While the work was underway, we learned through private communication from Dr. R. M. Archibald¹³ that he had a paper in press which contained several methods for the determination of alloxan. We would like to thank him for his courtesy in allowing us to read his manuscript before it appeared in print. Of those methods described by Archibald the most specific and sensitive is based on the condensation of alloxan with *o*-phenyl-

¹ The authors wish to express their appreciation to the Lederle Laboratories for a research grant that has aided greatly in this work. We are indebted to Dr. R. O. Roblin, Jr., of the American Cyanamid Company, for the sample of alloxan monohydrate used in these studies, and to Dr. J. A. Aeschlimann, of Hoffmann-La Roche, Inc., for a supply of 1,2-dimethyl-4-amino-5-(*d*-1'-ribityl-amino)-benzene.

² The authors also wish to acknowledge with appreciation the technical assistance of Miss Rachel Jewett and Miss Martha Fuchs.

³ J. S. Dunn, H. L. Sheehan and N. G. B. McLetchie, *Lancet*, 244: 484, 1943.

⁴ J. S. Dunn, J. Kirkpatrick, N. G. B. McLetchie and S. V. Telfer, *Jour. Path. Bact.*, 55: 245, 1943.

⁵ J. S. Dunn and N. G. B. McLetchie, *Lancet*, 245: 384, 1943.

⁶ C. C. Bailey and O. T. Bailey, *Jour. Am. Med. Assn.*, 122: 1165, 1943.

⁷ M. G. Goldner and G. Gomori, *Endocrinology*, 33: 297, 1943.

⁸ H. Hughes, L. L. Ware and G. F. Young, *Lancet*, 246: 148, 1944.

⁹ J. H. Ridout, A. W. Ham and G. A. Wrenshall, *SCIENCE*, 100: 57, 1944.

¹⁰ S. Banerjee, *Lancet*, 247: 658, 1944.

¹¹ E. P. Joslin, *New Eng. Jour. Med.*, 230: 425, 1944.

¹² E. P. Joslin, *New Eng. Jour. Med.*, 232: 219, 1945.

¹³ R. M. Archibald, *Jour. Biol. Chem.*, 158: 347, 1945.

enediamine to yield alloxazine, which is measured by its fluorescence.

In the test we are reporting in the present communication, we have employed the condensation of alloxan with 1,2-dimethyl-4-amino-5(*d*-1'-ribitylamino)-benzene(I) to yield riboflavin.¹⁴

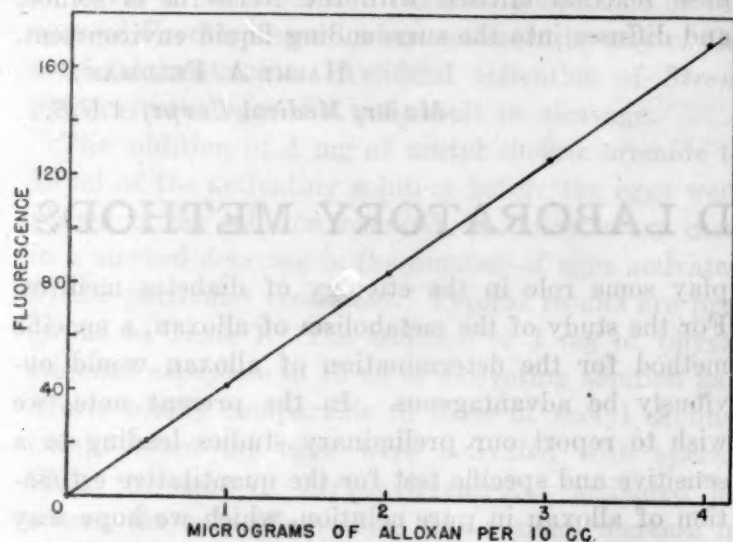


FIG. 1. Fluorescence of riboflavin plotted against the amounts of alloxan which were treated to yield riboflavin.

The riboflavin so produced was measured quantitatively by its fluorescence and by its growth-promoting properties for *Lactobacillus casei*. This method thus offers the high degree of specificity of the requirements for riboflavin by a microorganism as a check for the easily measured fluorescence of riboflavin. Furthermore, the already well-known methods for the determination of riboflavin are utilized.

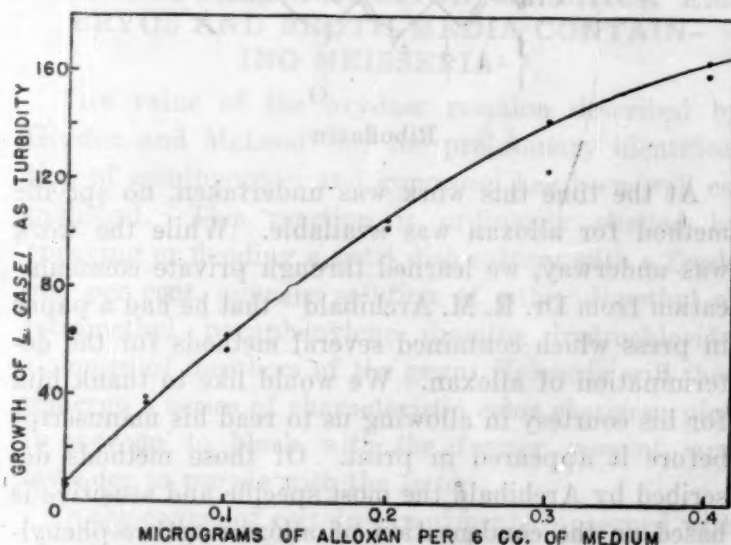


FIG. 2. Growth of *L. casei* plotted against the amounts of alloxan which were treated to yield riboflavin.

When alloxan in amounts from 0.2 to 4 micrograms per cc was treated as described under "Procedure," the fluorescence obtained was proportional to the amount of alloxan present (Fig. 1). A typical ribo-

¹⁴ R. Kuhn, K. Reinemund, F. Weygand and R. Ströbele, *Ber.*, 68: 1765, 1935.

flavin growth-response with *L. casei* was obtained with the riboflavin formed in the condensation. Amounts from 0.05 to 0.4 micrograms of alloxan converted to riboflavin could be measured by this microbiological procedure (Fig. 2).

Using our fluorescent method, we were able to confirm the results of Leech and Bailey¹⁵ on the stability of alloxan at various hydrogen ion concentrations (Fig. 3). Alloxan remained stable in glacial acetic

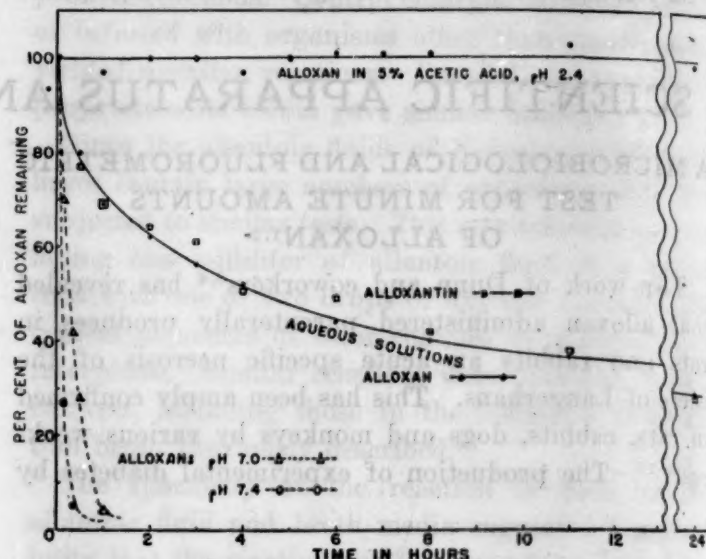


FIG. 3. Curves illustrating the stability of alloxan at various hydrogen ion concentrations, and a comparison of the stability of alloxan with alloxantin in aqueous solutions.

acid and in solutions of 5 per cent. acetic acid in water for a period of several weeks. Alloxantin, when treated with 1,2-dimethyl-4-amino-5(*d*-1'-ribitylamino)-benzene, yielded the same amount of riboflavin as did alloxan. The stability of alloxantin in water (10γ/cc) was also found to be identical with that of alloxan in water (Fig. 3).

Procedure: A stock solution of alloxan, containing 100 micrograms of alloxan per cc of 5 per cent. acetic acid in water, was prepared weekly. Solutions containing 10 and 1 micrograms per cc, respectively, were prepared daily by diluting the stock solution with 5 per cent. acetic acid. A sufficient amount of 1,2-dimethyl-4-amino-5(*d*-1'-ribitylamino)-benzene was dissolved in glacial acetic acid to give a concentration of 2 mg per cc.

To 20×150 mm pyrex test-tubes were carefully added the following amounts of alloxan: 0.2, 0.5, 1.0, 2.0, 3.0 and 4.0 micrograms; the volume in each tube was adjusted to 1.0 cc with water. Unknown solutions to be analyzed are likewise made up to 1 cc of volume. Then to each tube was added 1.0 cc of glacial acetic acid and 1.0 cc (2.0 mg) of 1,2-dimethyl-4-amino-5(*d*-1'-ribitylamino)-benzene. The tubes were

¹⁵ R. S. Leech and C. C. Bailey, *Jour. Biol. Chem.*, 157: 525, 1945.

heated simultaneously in a water bath (90–100°) for 3 hours. At the end of this period of heating, if the amount of alloxan present was to be measured fluorometrically, 8.0 cc of 1 M sodium acetate-acetic acid buffer, pH 5.5, were added to each tube. The fluorescence of the formed riboflavin was measured by a Coleman photofluorometer, Model 12, using the filters for riboflavin determinations supplied with the instrument. The degree of fluorescence is plotted against concentration of the standard alloxan solutions as shown in Fig. 1.

The concentration of alloxan in the unknown solutions, run simultaneously with the standards, is obtained from the plotted curve. If the amount of riboflavin formed from the alloxan was to be measured by its effect on the growth of *Lactobacillus casei*, then the contents of the tubes after heating on the water bath were carefully concentrated to dryness. This was accomplished rapidly by evaporating the solutions under vacuum of a water pump while at the same time the tube was shaken with a swirling motion in a hot water bath. Standard and unknown samples were treated under identical conditions. Immediately after the solutions were concentrated to dryness, the residue was dissolved in exactly 10 cc of 0.2 M sodium acetate-acetic buffer, pH 6.6. One cc of each of these solutions was then added to 5.0 cc of the medium developed by Landy and Dicken,¹⁶ which needed only riboflavin for good growth of *Lactobacillus casei*. After sterilization, each tube was inoculated with one drop of a 1:20 dilution of a 24-hour culture of *L. casei* grown in the basal medium; the cells were centrifuged and resuspended in a sterile saline solution before the final inoculum dilution was made. After 40 hours of incubation at 37°, the growth of *L. casei* was measured turbidimetrically in a Klett-Summerson photoelectric colorimeter. The growth response of *L. casei* to increasing amounts of alloxan is plotted in Fig. 2.

SUMMARY

A microbiological and fluorometric test for the determination of minute amounts of alloxan has been described. The test involves the conversion of the alloxan to riboflavin which is measured by microbiological or fluorometric techniques.

SACHCHIDANANDA BANERJEE¹⁷

KARL DITTMER

VINCENT DU VIGNEAUD

DEPARTMENT OF BIOCHEMISTRY,
CORNELL UNIVERSITY MEDICAL COLLEGE,
NEW YORK, N. Y.

¹⁶ M. Landy and D. M. Dicken, *Jour. Lab. Clin. Med.*, 27: 1086, 1942.

¹⁷ Ghosh Traveling Fellow of the University of Calcutta.

A HANGING DROP METHOD FOR CONTINUOUS OBSERVATION OF THE ACTIVITY OF ORGANISMS IN CYANIDE¹

INTERPRETATION of cellular oxidative processes may be aided by correlating the oxygen consumption of organisms exposed to cyanide with observations of their visible activity. With the method described it is possible to observe cell division, muscle contraction and other phenomena, while the concentration of HCN is varied quantitatively and the organisms remain otherwise undisturbed. The procedure is possible because of the rapid diffusion of HCN gas and the consequent rapid attainment of equilibrium between a large volume of cyanide solution of a known concentration and a hanging drop exposed to it.

Fig. 1 illustrates the transparent plastic chamber

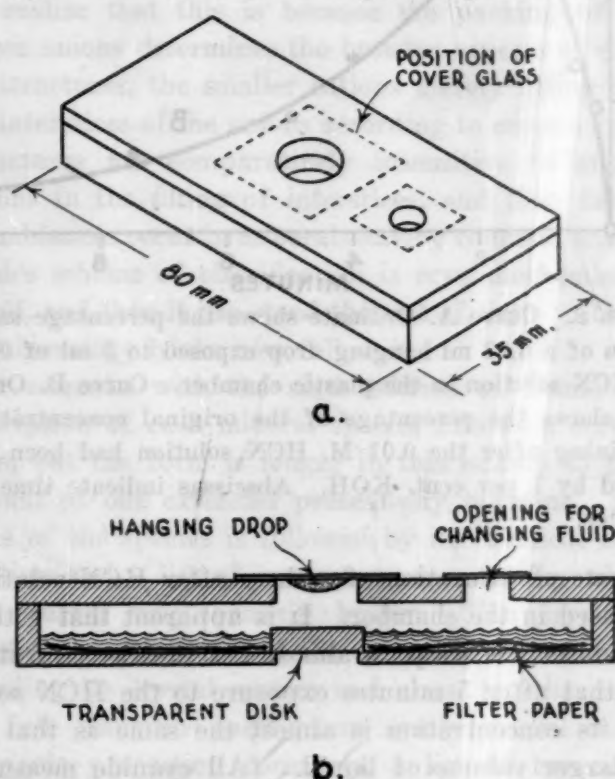


FIG. 1. Transparent plastic chamber used in observing effect of cyanide on behavior of organisms in a hanging drop. A. Isometric view. B. Longitudinal section.

designed for these experiments. The top and bottom plates are sealed together with liquid petrolatum and a cover glass with a hanging drop containing the tissue or organism is set over the opening as shown. After a control period in which the normal behavior is noted, 3 ml of HCN solution made up in the same medium as the hanging drop is placed on the filter paper in the chamber and the small opening is closed. In a short time the HCN concentration in the drop becomes the same as that in the larger volume of fluid, and since the plastic is relatively impermeable it will stay at this level for hours without change. It is thus possible to attain a given level of cyanide

¹ From the Department of Ophthalmology, State University of Iowa, College of Medicine.

without altering the position of the organism or disturbing its ionic environment. The saturation of a 0.03 ml drop depletes the 3 ml of solution in the chamber by only 1 per cent. Fig. 2, curve A, shows

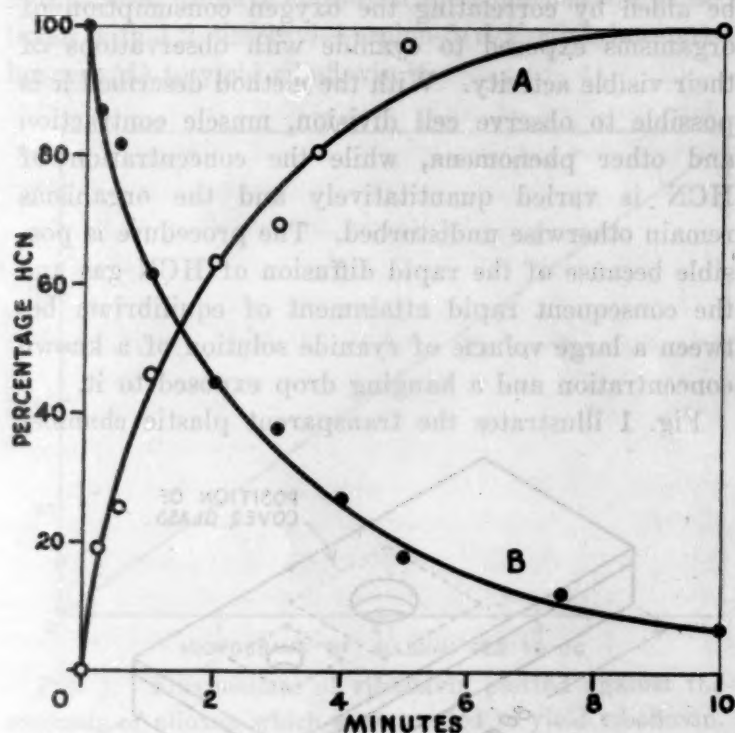


FIG. 2. Curve A. Ordinate shows the percentage saturation of a 0.03 ml hanging drop exposed to 3 ml of 0.01 M. HCN solution in the plastic chamber. Curve B. Ordinate shows the percentage of the original concentration remaining after the 0.01 M. HCN solution had been replaced by 1 per cent. KOH. Abscissas indicate time in minutes.

the rate of saturation of a drop after HCN solution is placed in the chamber. It is apparent that within 2 minutes the drop is almost two thirds saturated, and that after 5 minutes exposure to the HCN solution its concentration is almost the same as that of the larger volume of liquid. (All cyanide measurements were made by the phenolphthalin method.²)

It is an equally simple process to watch the recovery from cyanide treatment. When the HCN solution is removed from the chamber with a pipette and replaced with a 1 per cent. KOH solution, the cyanide

in the drop quickly passes into the alkali and leaves the drop in its original condition. As shown by curve B in Fig. 2, the concentration in the drop decreases 50 per cent. within 2 minutes after the replacement with KOH, and is less than one fifth of the original level in 5 minutes.

The cyanide solutions are prepared by dissolving a weighed amount of KCN in a volumetric flask, neutralizing it with dilute HCl (with a drop of phenol red as indicator), and diluting this stock solution to make the concentrations desired. Although it is theoretically preferable to make these solutions from liquid of the same pH and osmotic pressure as the medium of the hanging drop, there is actually very little difference in the HCN tension within a range of pH 6.8 to 7.4 and a salinity of 0 to 5 per cent. With sea water experiments the cyanide solutions should be prepared with sea water.

Three sample experiments suggest the possible uses of the method. (1) *Vorticella*: These protozoons placed in a hanging drop of pond water and exposed to 0.04 M. HCN were immediately stimulated and most of them became free-swimming, but in spite of the high concentration the majority of the animals were still alive after an hour. (2) *Artemia*: Brine shrimp in artificial sea water showed a marked variation in sensitivity with age, perhaps associated with the type of substrate being metabolized. Young animals were still living after an hour in 0.01 M. HCN, but older ones became inactive in 10 minutes with only 0.001 M. HCN. (3) *Ciliated Epithelium*: Cilia on sections of rat trachea suspended in buffered saline will beat for hours at room temperature. A concentration of 0.0003 M. HCN stopped most of this action in 5 minutes, but with 0.0001 M. it was only slightly slowed after half an hour. After the activity had been arrested by 0.01 M. HCN, the solution in the chamber was replaced with 1 per cent. KOH. Enough recovery occurred in 15 minutes to permit motion to start again, and by half an hour the ciliary activity appeared normal.

WILBUR ROBBIE

SCIENTIFIC BOOKS

MINERALOGY

Dana's System of Mineralogy. By CHARLES PALACHE, HARRY BERMAN and CLIFFORD FRONDEL. Seventh Edition, Volume I, Elements, Sulfides, Sulfosalts, Oxides. New York: John Wiley and Sons, Inc., 1944. \$10.00.

DANA'S System of Mineralogy is America's most important compilation of information on mineral species, and has been a reference standard for about a

² W. A. Robbie, *Arch. Biochem.*, 5: 49, 1944.

century. It holds a place of authority in mineralogy somewhat analogous to that of Gray's Manual in the field of botany. The last edition of the System appeared in 1892, and supplements to it were published in the form of Appendices in 1899, 1909 and 1915. Since these appeared x-ray diffraction has been developed into a new tool with which to study crystals generally, and has been intensively applied to the study of minerals. The science of mineralogy has been greatly enriched by its aid, not only in sheer

weight of new data, but also in the new perspective which the study and correlation of such new data have made possible. Naturally, mineralogists have awaited eagerly a new edition of the System in which the new data and the new viewpoints would be incorporated.

This edition of Dana's System is more than just a revision. The authors have not limited themselves to adding to the old edition new data which subsequently had appeared in the literature. Rather, they regarded the opportunity of revision as a challenge to initiate a large-scale research project concerned with the investigation of any little-known or doubtful species or families of minerals. In this aspect of the "revision" they did not hesitate to enroll their colleagues. Their chief task was the critical sifting and rearranging of all the resulting old and new data. The final result was a new work, which is the old Dana only in aim and excellence. To carry out this unusual type of revision in all its aspects, the authors were aided by a grant from the Penrose Fund of the Geological Society of America.

The authors of this revision, Professor Charles Palache, the late Professor Harry Berman and Dr. Clifford Frondel, all members of Harvard's Department of Mineralogy, composed an excellent team for their project, for this combination assured a command of traditional mineralogy and crystallography together with a conversancy with the newer x-ray crystallography and its offspring, crystal chemistry. The combination has produced a work which thus bridges the old and the new in mineralogy. The mineralogical fraternity may congratulate itself that in the new Dana they thus have a bridge and not just one side or the other of a hiatus.

This volume represents the first of a series of three. It is devoted to the elements, sulfides, sulfosalts and oxides (excluding silica). The arrangement of material is chemical. Thus the species are first arranged according to the following chemical "classes": (1) Native elements; (2) Sulfides, selenides and tellurides; (3) Sulfosalts; (4) Simple oxides (exclusive of silica); (5) Oxides containing uranium, thorium and zirconium; (6) Hydroxides, and oxides containing hydroxyl; (7) Multiple oxides [such as $MgAl_2O_4$]; (8) Multiple oxides containing columbium, tantalum and titanium. These "classes" are further subdivided into "types" according to the ratio of cations to anions in the chemical formula. For example, the simple oxides are divided into the following "types": M_2O , MO , M_3O_4 , M_2O_3 , MO_2 (exclusive of SiO_2) and miscellaneous M_mO_n .

This scheme of classification, now familiar in its broader aspects to all American mineralogists, is an elaboration of the general chemical classification so

successfully utilized in previous editions of Dana, and dating from the fifth edition by Dana and Brush, published in 1868. Dana's chemical classification was characterized by arrangement according to common anion, in contrast with the scheme whereby minerals are arranged primarily according to a common cation. The latter system, sometimes adopted because it places together all minerals containing copper, for example, is an unnatural one except for economic purposes. Its use hinders rather than helps the scientific study of minerals, since it places together minerals having no common crystallographic features. Dana's common anion classification, on the other hand, has been successful because it groups together minerals with related crystal features. In the light of the crystallochemical knowledge now available to us, we realize that this is because the packing of the larger anions determines the broader aspects of crystal structures, the smaller cations merely fitting into the interstices of the anions according to certain rules. Structures are comparatively insensitive to substitutions in the filling of interstices, and thus family resemblances occur in minerals having common anions. Dana's scheme of classification is crystallochemically sound, and thus it has stood the test of time. Almost all mineralogy books now follow it.

In common with the sixth edition of Dana, the description of each mineral species follows a certain form, but the form is longer in this edition to take account of our extended present-day horizons. The name of the species is followed by its chemical composition and a list of synonyms or names by which the mineral was formerly known. The crystallographic characteristics of the species are next listed, including its crystal system and class, together with the full Mauguin point-group symbol, axial ratio, gnomonic projection constants, a list of two-circle goniometer coordinates of known forms and cell constants derived from x-ray diffraction studies. Then follow discussions and lists of data under the headings of physical properties, optical constants, chemical composition (including representative analyses), occurrence, alterations, artificial production of the species and a brief section on the origin of the mineral name.

An important feature of the new Dana is that references are given to at least the most recent investigations of each mineral species. This enables the research mineralogist to gain an introduction to the literature of a species through its most recent contributions. In this edition of Dana the references are better arranged than in older editions, and they are annotated and interspersed with valuable critical comments by the authors.

The introductory section on crystallography is not

well treated. Some thirty-odd pages are devoted to "morphological crystallography," chiefly in its computing aspects, and the rest of the science of crystallography is compressed into some four pages. This leaves much of the subject untouched. For example, a discussion of the plastic behavior of minerals, a topic now of great interest in several advancing research fronts, is missing. Certainly this section presents an ill-balanced account of the crystallographic aspects of mineralogy, and might better have been omitted than treated as it is.

The reviewer would hesitate to criticize the authors' choice of fonts for headings except for the fact that two more volumes of this work are yet to appear, and they could be made much more readable by a different selection of headings. Properly chosen, headings divide the work into coordinate and subordinate parts whose relative ranks are obvious. In this volume, however, headings of four different ranks are all printed in bold face type of approximately 10 point size. These are differentiated only by use of capitals and italics, all of which look much alike in heavy type. The reviewer suggests that in subsequent volumes of Dana's System, the authors follow the excellent style set in the 1932 edition of Dana-Ford's "Textbook," which is a condensation of the System.

These two criticisms are trivial compared with the solid virtues of the book. Nowhere else can the mineralogist find such a complete or up-to-date compilation and arrangement of mineral species data. The authors are to be congratulated on a splendid achievement and on performing a welcome service. Among other things, this volume will stand as a monument to one of the co-authors, the late Dr. Harry Berman, who lost his life in an aircraft accident while serving the Allied cause in his chosen field of mineralogy.

M. J. BUEGER

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

FRESH-WATER SNAILS

The Molluscan Family Planorbidae. By FRANK COLLINS BAKER. (Collation, revision and additions by Harley Jones Van Cleave.) xxxvi+530 (including 141 plates) + 1 portrait. Urbana: University of Illinois Press. 1945. \$14.50.

To this taxonomic monograph, the late F. C. Baker has contributed the magnificently figured results of years of dissection and of microscopic study of radulae, in addition to photographs of the shells of most American forms and of examples of the foreign genera. On the basis of these new data, collated with those of other students, the Planorbidae of the world, after exclusion of the Bulinidae, are divided into 4 subfamilies and 34 genera: Planorbulinae with 12, Segmentininae with 11, Helisomatinae with 7 and

Planorbulinae with 4 genera. *Choanomphalus* (Choanomphalinae) and *Poecilospira* are considered "groups of uncertain affinities." All the divisions are defined carefully, with lists of "valid" forms and notes on distribution. Although opinions may vary in regard to the generic rank of some of these groups, their content and relationships are carefully worked out, so far as present knowledge permits. A chapter on general ecology discusses planorbids as intermediate hosts for trematodes.

A principal difficulty is that the wealth of new and compiled data, in this indispensable reference book, is indexed imperfectly, probably due to F. C. Baker's untimely death. Especially in such a thorough revision, with so many new or unfamiliar combinations, the lack of an alphabetic list of the specific and sub-specific terms forces a perusal of all the book to find in what genera the forms, most of which were described in *Planorbis*, are now included. In addition, the nine new species and seventeen varieties described in part 13, and several of the names which appear in the plate explanations, are omitted from the systematic account. In this connection, the author probably meant to put *Menetus coloradoensis* (p. 230) in *Promenetus* (p. 178). Also, *Tropicorbis orbiculus dunkeri*, a "new name" (p. 494) is not included in the index to new forms but appears only in the plate index, and then under *T. obstructus*. Incidentally, the "index to text" lists seventeen "new varieties" (p. 525) but only fourteen "varieties, new" (p. 526). Misspellings are fairly infrequent, although they include fourteen species names in *Gyraulus* (pp. 66-71). But, despite these minor defaults of taxonomic desuetude, Van Cleave, with his interesting biography, careful bibliography and fine portrait, has shaped an admirable monument to an eager investigator and inspiring friend.

HORACE B. BAKER

UNIVERSITY OF PENNSYLVANIA

BOOKS RECEIVED

- BEALS, RALPH L., GEORGE W. BRAINERD and WATSON SMITH. *Archaeological Studies in Northeast Arizona.* Illustrated. Pp. x+171. University of California Press. 1945.
- HUNTINGTON, ELLSWORTH. *Mainsprings of Civilization.* Illustrated. Pp. xii+660. John Wiley and Sons, Inc. \$4.75. 1945.
- RICHARDS, I. A., and CHRISTINE GIBSON. *Learning Basic English.* Pp. 116. W. W. Norton & Company, Inc. \$2.00. 1945.
- SHREVE, R. NORRIS. *The Chemical Process Industries.* Illustrated. Pp. xiii+957. McGraw-Hill Book Company. \$6.00. 1945.
- VERDOORN, FRANS. *Plants and Plant Science in Latin America.* Illustrated. Pp. xxxvii+381. Chronica Botanica Co., Waltham, Mass. \$6.00. 1945.
- WARNER, W. LLOYD, and LEO SROLE. *Yankee City Series, Vol. III: The Social Systems of American Ethnic Groups.* Pp. xii+318. Yale University Press. \$4.00. 1945.